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Culprit Vessel–Only Versus Multivessel Percutaneous Coronary Intervention in Patients With Cardiogenic Shock Complicating ST-Segment–Elevation Myocardial Infarction

A Collaborative Meta-Analysis

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Background—The optimal revascularization strategy in patients with multivessel disease presenting with cardiogenic shock complicating ST-segment–elevation myocardial infarction remains unknown.

Methods and Results—Databases were searched from 1999 to October 2016. Studies comparing immediate/single-stage multivessel percutaneous coronary intervention (MV-PCI) versus culprit vessel–only PCI (CO-PCI) in patients with multivessel disease, ST-segment–elevation myocardial infarction, and cardiogenic shock were included. Primary end point was short-term (in-hospital or 30 days) mortality. Secondary end points included long-term mortality, cardiovascular death, reinfarction, and repeat revascularization. Safety end points were in-hospital stroke, renal failure, and major bleeding. The meta-analysis included 11 nonrandomized studies and 5850 patients (1157 MV-PCI and 4693 CO-PCI). There was no significant difference in short-term mortality with MV-PCI versus CO-PCI (odds ratio [OR], 1.08; 95% confidence interval [CI], 0.81–1.43; *P*=0.61). Similarly, there were no significant differences in long-term mortality (OR, 0.84; 95% CI, 0.54–1.30; *P*=0.43), cardiovascular death (OR, 0.72; 95% CI, 0.42–1.23; *P*=0.23), reinfarction (OR, 1.65; 95% CI, 0.84–3.26; *P*=0.15), or repeat revascularization (OR, 1.13; 95% CI, 0.76–1.69; *P*=0.54) between the 2 groups. There was a nonsignificant trend toward higher in-hospital stroke (OR, 1.64; 95% CI, 0.98–2.72; *P*=0.06) and renal failure (OR, 1.30; 95% CI, 0.98–1.72; *P*=0.06), with no difference in major bleeding (OR, 1.47; 95% CI, 0.39–5.63; *P*=0.57) with MV-PCI when compared with CO-PCI.

Conclusions—This meta-analysis of nonrandomized studies suggests that in patients with cardiogenic shock complicating ST-segment–elevation myocardial infarction, there may be no significant benefit with single-stage MV-PCI compared with CO-PCI. Given the limitations of observational data, randomized trials are needed to determine the role of MV-PCI in this setting. **(*Circ Cardiovasc Interv*. 2017;10:e005582. DOI: 10.1161/CIRCINTERVENTIONS.117.005582.)**

Key Words: cardiogenic shock ■ complete revascularization ■ mortality ■ myocardial infarction ■ percutaneous coronary intervention ■ stroke

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WHAT IS KNOWN

- Recent data from randomized controlled trials have shown that in patients with ST-segment–elevation myocardial infarction without cardiogenic shock, multivessel percutaneous coronary intervention (MV-PCI) compared with culprit vessel–only PCI is associated with improved clinical outcomes, but mainly driven by less repeat revascularization.
- No randomized data exist on MV-PCI versus culprit vessel–only PCI in patients with cardiogenic shock, and observational studies have produced conflicting results.

WHAT THE STUDY ADDS

- In this meta-analysis of 11 nonrandomized studies including 5850 patients with multivessel disease, ST-segment–elevation myocardial infarction, and cardiogenic shock, there were no significant differences in short-term mortality, long-term mortality, cardiovascular death, reinfarction, or repeat revascularization with immediate/single-stage MV-PCI versus culprit vessel–only PCI.
- There was a nonsignificant trend toward higher in-hospital stroke and renal failure, but no difference in major bleeding with MV-PCI compared with culprit vessel–only PCI.
- Given the limitations of observational data, randomized trials are needed to determine the role of MV-PCI in patients with cardiogenic shock complicating ST-segment–elevation myocardial infarction.

Cardiogenic shock occurs in 6% to 12% of patients with ST-segment–elevation myocardial infarction (STEMI) and is associated with increased mortality.[1–3] The SHOCK trial (Should We Emergently Revascularize Occluded Coronaries for Cardiogenic Shock) demonstrated improved short- and long-term survival with early revascularization in patients with acute myocardial infarction (MI) and cardiogenic shock.[4,5] However, despite the increasing use of percutaneous coronary intervention (PCI) in these patients, mortality remains high at 40% to 50%.[2]

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Multivessel coronary artery disease is present in ≤80% of patients with cardiogenic shock complicating STEMI and is associated with worse outcomes.[4,6] Recent data from randomized controlled trials (RCTs) have shown that in patients with STEMI without cardiogenic shock, multivessel PCI (MV-PCI) compared with culprit vessel–only PCI (CO-PCI) is associated with improved clinical outcomes, but mainly driven by less repeat revascularization.[7–10] However, no randomized data exist on MV-PCI versus CO-PCI in patients with cardiogenic shock. The 2013 American College of Cardiology Foundation/American Heart Association guidelines for the management of STEMI suggests that in patients with cardiogenic shock because of pump failure, PCI of a severe stenosis in a large noninfarct artery might improve hemodynamic stability and should be considered during the primary procedure.[11] Similarly, the 2014 European Society of Cardiology/European Association for Cardio-Thoracic Surgery guidelines on myocardial revascularization state that multivessel PCI during STEMI should be considered in patients with cardiogenic shock in the presence of multiple, critical stenoses or highly unstable lesions (angiographic signs of possible thrombus or lesion disruption), and if there is persistent ischemia after PCI on the supposed culprit lesion.[12] These recommendations are largely based on theoretical considerations and extrapolation of clinical trial data in hemodynamically stable STEMI patients, but not on nonrandomized studies in patients with cardiogenic shock. However, observational studies comparing MV-PCI versus CO-PCI in patients with cardiogenic shock have produced conflicting results, and the optimal revascularization strategy in these patients remains unknown.[1,6,13–22] In addition, several observational studies have included patients with STEMI and non-STEMI, and evidence suggests that clinical profile, treatment, and outcomes are different in these 2 groups of patients.[1,3,6,15,16,22] Furthermore, prior meta-analyses comparing MV-PCI versus CO-PCI have included studies in patients with or without shock.[23,24] Hence, the primary objective of our study was to perform a systematic review and meta-analysis of studies comparing clinical outcomes of MV-PCI versus CO-PCI specifically in patients with cardiogenic shock complicating STEMI.

Methods

Data Sources

We searched PubMed, MEDLINE (Medical Literature Analysis and Retrieval System Online), CINHAL (Cumulative Index to Nursing and Allied Health Literature), Cochrane CENTRAL (Central Register of Controlled Trials), EMBASE (Excerpta Medica Database), Web of Science, and Google Scholar from August 1999 (publication of the pivotal SHOCK trial which demonstrated improved survival with early revascularization in patients with acute MI and cardiogenic shock) through October 2016 for English language, peer-reviewed publications. Conference proceedings for the Scientific Sessions of the American College of Cardiology, American Heart Association, European Society of Cardiology, Transcatheter Cardiovascular Therapeutics, and EuroPCR (Congress of the European Association of Percutaneous Cardiovascular Interventions) were also searched. The following key words and Medical Subject Headings (MeSH) terms were used: cardiogenic shock, shock, cardiogenic (MeSH), myocardial infarction (MeSH), percutaneous coronary intervention (MeSH), percutaneous transluminal coronary angioplasty (MeSH), myocardial revascularization (MeSH), multivessel, multi-vessel, culprit vessel, culprit-only, non-infarct, and complete revascularization. Reference lists of review articles, meta-analyses, and original studies identified by the electronic search were reviewed to find other potentially eligible studies. Authors of studies were contacted when results were unclear, relevant data were not reported, or additional data were needed.[1,6,13,15–18,20,22]

Study Selection

Eligible studies had to fulfill the following criteria for inclusion in the meta-analysis: (1) study (sub)group included patients with STEMI, multivessel disease (MVD), and cardiogenic shock, (2) compared CO-PCI versus immediate/single-stage MV-PCI, (3) included at least 10 patients in each treatment group, (4) >50% of the patients underwent stent placement, and (5) at least in-hospital/30-day mortality data (number of events or event rates) for the 2 treatment groups were reported or provided by the authors on request. Because there are no randomized

studies comparing MV-PCI versus CO-PCI in patients with STEMI and cardiogenic shock, only nonrandomized studies and post hoc analyses of RCTs were included in this meta-analysis. We followed the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) and MOOSE (Meta-Analysis of Observational Studies in Epidemiology) checklists for the protocol of our meta-analysis.[25]

Data Extraction and Quality Assessment

Two physician reviewers (D.K. and P.S.) independently assessed study eligibility, quality, and extracted data. Disagreements were resolved by consensus. Study quality was evaluated using the Newcastle Ottawa Scale, which assigns a star for 3 areas of study quality: selection (4 criteria), comparability (1 criterion), and outcome (3 criteria; Table I in the Data Supplement).[26] Data were extracted from eligible studies on study design, baseline clinical characteristics, procedural details, and outcomes. Propensity-matched or inverse probability weight–adjusted data were used for the outcomes when available.

End Points

The primary end point was short-term (in-hospital or 30 days) all-cause mortality. Secondary end points included long-term (longest study follow-up) mortality, cardiovascular death, reinfarction, and repeat revascularization. Safety end points included in-hospital stroke, major bleeding, and renal failure.

Statistical Analysis

Random-effects models of DerSimonian and Laird were used to calculate pooled odds ratio (OR) and corresponding 95% confidence interval (CI) for each of the end points. Heterogeneity was assessed using the Higgins I^2 statistic, with values <25% and >75% considered indicative of low and high heterogeneity, respectively. Publication bias was assessed visually by asymmetry in funnel plots and formally using Egger regression test and Begg and Mazumdar rank correlation test. We performed sensitivity analysis after excluding single-center studies, studies with <50% drug-eluting stent use, and studies with <1 year follow-up. Chronological cumulative meta-analyses were performed to determine whether the effect size and precision would shift based on the changes in treatments over the course of time. Because individual studies included data over several years, the chronological order was based on the earliest year of the study period. We also conducted meta-regression analysis exploring the potential for effect modification by multiple variables including age, female sex, diabetes mellitus, chronic kidney disease, prior MI, prior coronary artery bypass grafting, left ventricular ejection fraction <40%, cardiac arrest (pre- or intraprocedure), left main/left anterior descending coronary artery as culprit vessel, stent use, drug-eluting stent use, and intra-aortic balloon pump use on the primary end point of short-term mortality. All results are for MV-PCI compared with CO-PCI. All tests were 2-tailed with a P value of <0.05 considered significant. Analyses were performed using the Review Manager Version 5.3 (The Nordic Cochrane Center, The Cochrane Collaboration, 2014, Copenhagen, Denmark) and Comprehensive Meta-Analysis Version 3.0 (Biostat, Englewood, NJ).

Results

Study Selection and Description of Included Studies

The database search yielded 946 articles of which 48 full-text articles were assessed for eligibility (Figure 1). Conference abstracts for which full text was not published were excluded to ensure high-quality data. Finally, 11 studies were included in the meta-analysis. The characteristics of the included studies are shown in the Table. Of the 11 studies, 6 were retrospective, 4 were prospective, and 1 was a post hoc analysis of a RCT. Of the 10 nonrandomized studies, 8 were from national, multicenter registries, and 2 were single-center studies. In majority of the studies,[1,14,16,17,19–22] MVD was defined as ≥50% stenosis in ≥2 major epicardial coronary arteries, except 2 studies[6,18] which used ≥70% as the cutoff, and 2 studies[13,15] that did not provide the exact cutoff used. The 11 studies included 5850 patients with STEMI, MVD, and cardiogenic shock. Of these, 4693 (80.2%) underwent CO-PCI and 1157

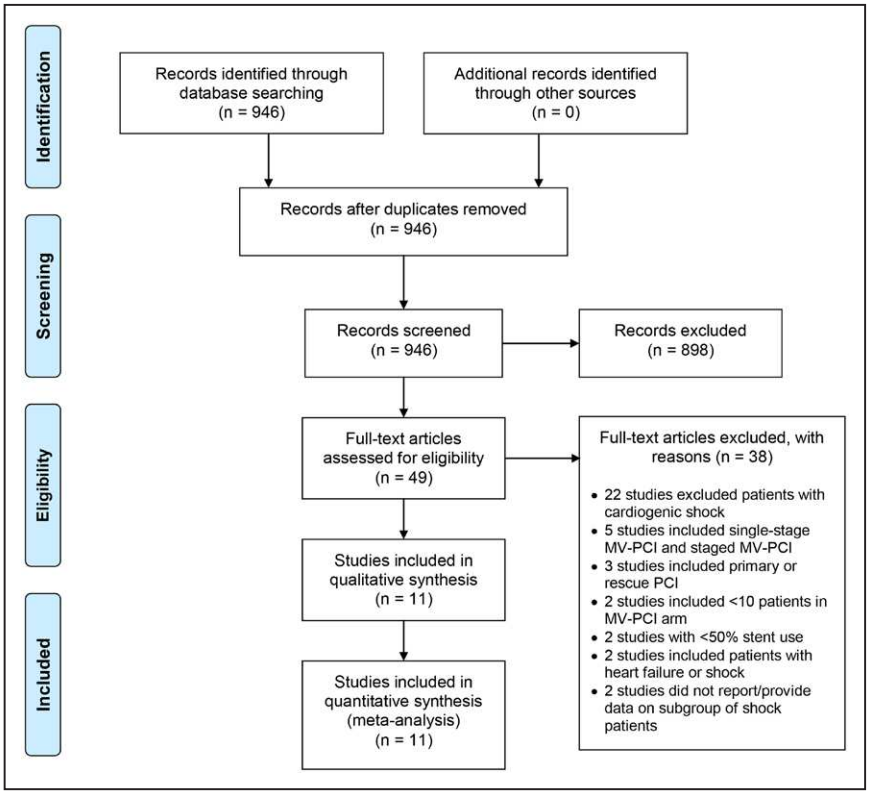

Figure 1. PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) selection flow diagram. MV-PCI indicates multivessel percutaneous coronary intervention.

Table. Characteristics of the 11 Included Studies

Study	Data Source	Study Period	Study Design	n*	Definition of MVD	Definition of Cardiogenic Shock	Exclusion	Outcome(s)	Follow-Up
Bauer et al[6] 2012	EHS-PCI	2005–2008	Retrospective	278	≥70% stenoses of ≥2 major epicardial vessels	SBP ≤90 mm Hg for ≥30 min or inotropes needed to maintain SBP >90 mm Hg and evidence of end-organ hypoperfusion and increased filling pressures	LM, prior CABG	All-cause mortality	In-hospital
Cavender et al[13] 2009	ACC-NCDR	2004–2007	Retrospective	3087	CAD in >1 major artery	SBP <80 mm Hg and a CI <1.8 despite maximal treatment or requiring intravenous inotropes and an IABP to maintain the SBP at >80 mm Hg and the CI at >1.8 L min^{-1} m^{-2}	LM, staged MV-PCI, thrombolytics	All-cause mortality, stroke, renal failure, bleeding	In-hospital
Cavender et al[14] 2013	Single center	2002–2010	Retrospective, propensity matched	64	≥50% stenosis in ≥2 major epicardial coronary arteries	SBP <90 mm Hg, and CI <2.2 L min^{-1} m^{-2}, and parenteral inotropic or vasopressor agents or mechanical support needed to maintain SBP and CI above those specified levels	Definite indications for surgery (eg, significant valvular heart disease, mechanical complications of MI)	All-cause mortality	5 y†
Hambraeus et al[15] 2016	SWEDEHEART (SCAAR)	2006–2010	Prospective	310	NA	NA	Single-vessel disease, prior CABG	Composite of all-cause death, MI, repeat revascularization	12 mo
Jaguszewski et al[16] 2013 (Jeger et al[17] 2014)‡	AMIS Plus	2005–2012	Retrospective	243	≥50% in ≥2 main coronary arteries and involving the LM	Killip class IV	NA	MACCE, all-cause mortality, MI, stroke	In-hospital (1-year mortality data on 70 patients†)
Mylotte et al[18] 2013	Multicenter	1998–2010	Prospective	169	≥70% stenosis in a major (≥2.5-mm diameter) non-IRA, or distal LM lesion with significant stenosis of the ostia of both the daughter arteries	SBP <90 mm Hg for >30 min or the requirement for supportive measures to maintain SBP >90 mm Hg, and evidence of end-organ hypoperfusion (cool extremities, urine output <30 mL/h, and a heart rate ≥60 bpm) after survived out-of-hospital cardiac arrest	Late presentation (>24 h), staged MV-PCI	All-cause mortality, death because of cardiogenic shock, recurrent cardiac arrest, composite of these end points	6 mo
Park et al[19] 2015	KAMIR	2006–2012	Prospective, inverse probability of treatment weighting	319	≥50% diameter stenosis in at least 1 major nonculprit vessel	SBP <90 mm Hg for >30 min or the need for supportive management to maintain SBP ≥90 mm Hg and evidence of end-organ hypoperfusion (cool extremities, urine output <30 mL/h or altered mental status)	Missing initial vital signs information, NSTEMI	All-cause mortality, cardiac death, MI, revascularization, MACE	Median 194 d (IQR, 14–374 d)
van der Schaaf et al[20] 2010	Single center	1997–2005	Retrospective	161	≥1 stenosis >50% of the coronary lumen diameter in ≥1 of the non-IRA epicardial arteries or LM stenosis ≥50%	SBP ≤90 mm Hg for ≥30 min or vasopressors required to maintain SBP >90 mm Hg, evidence of end-organ hypoperfusion (eg, urine output <30 mL/h or cold/diaphoretic extremities orv altered mental status), and evidence of elevated filling pressures (eg, pulmonary congestion on examination or chest x-ray)	NA	All-cause mortality	1 y

(*Continued*)

Table. Continued

Study	Data Source	Study Period	Study Design	n*	Definition of MVD	Definition of Cardiogenic Shock	Exclusion	Outcome(s)	Follow-Up
Yang et al[21] 2014	KAMIR and KWGMI	2005–2010	Prospective	338	≥50% stenosis in at least 1 major non-IRA	SBP <90 mm Hg or vasopressors required to maintain a SBP >90 mm Hg; signs of hypoperfusion (eg, urine output <30 mL/h or cold/diaphoretic extremities or an altered mental status); and clinical evidence of elevated left ventricular filling pressure (eg, pulmonary congestion on physical examination or chest radiograph)	Treatment strategy other than primary PCI, mechanical complications of MI, LM	All-cause mortality, cardiac death, cardiac death or recurrent MI, any revascularization, MACE	Median 224 d (IQR, 46–383 d)
Zeymer et al[1] 2015	ALKK-PCI	2008–2011	Retrospective	555	>50% stenosis of 2 or 3 major vessels	SBP <90 mm Hg, heart rate >100 bpm and clinical signs of end-organ hypoperfusion, such as cold, clammy skin, oliguria, altered mental status or elevated serum lactate	LM, prior CABG	All-cause mortality, nonfatal MI, stroke, bleeding, dialysis	In-hospital
Zeymer et al[22] 2016	IABP-SHOCK II	2009–2012	Post hoc analysis of RCT	306	>50% stenosis in ≥2 major coronary vessels	SBP <90 mm Hg for >30 min or catecholamines required to maintain SBP >90 mm Hg plus clinical signs of pulmonary congestion and signs of impaired organ perfusion with at least one of the following: altered mental status; cold, clammy skin, and extremities; oliguria with urine output <30 mL/h; serum lactate >2.0 mmol/L	Resuscitation >30 min, severe cerebral deficit, mechanical cause of shock, onset of shock >12 h, shock of other cause, severe PAD or AI, age >90 y, life expectancy <6 mo	30-day all-cause mortality, 6-and 12-month mortality, reinfarction, renal replacement therapy, GUSTO moderate, severe, or life-threatening bleeding	12 mo

ACC-NCDR indicates American College of Cardiology National Cardiovascular Data Registry; AI, aortic insufficiency; ALKK-PCI, Arbeitsgemeinschaft Leitende Kardiologische Krankenhausärzte-PCI registry; AMIS Plus, Acute Myocardial Infarction in Switzerland Plus Registry; CABG, coronary artery bypass grafting; CAD, coronary artery disease; CI, cardiac index; EHS-PCI, Euro Heart Survey PCI Registry; GUSTO, Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Coronary Arteries trial; IABP-SHOCK II, Intra-Aortic Balloon Pump in Cardiogenic Shock II; IQR, interquartile range; IRA, infarct-related artery; KAMIR, Korean Acute Myocardial Infarction Registry; KWGMI, Korea Working Group on Myocardial Infarction registry; LM, left main coronary artery; MACCE, major adverse cardiovascular and cerebrovascular event; MACE, major adverse cardiovascular events; MI, myocardial infarction; MV-PCI, multivessel PCI; MVD, multivessel disease; NA, not available or not specified; NSTEMI, non–ST-segment–elevation myocardial infarction; PAD, peripheral artery disease; PCI, percutaneous coronary intervention; RCT, randomized controlled trial; SBP, systolic blood pressure; SCAAR, Swedish Coronary Angiography and Angioplasty Registry; SHOCK, Should We Emergently Revascularize Occluded Coronaries for Cardiogenic Shock; and SWEDEHEART, Swedish Web-System for Enhancement and Development of Evidence-Based Care in Heart disease Evaluated According to Recommended Therapies.

*Included in the meta-analysis. The actual number of patients in the original study may be different.

†Only 1-year follow-up data were used in the current meta-analysis.

‡One-year mortality data were available for 70 patients included in the 2005 to 2012 AMIS Plus study cohort (Jeger et al[17]).

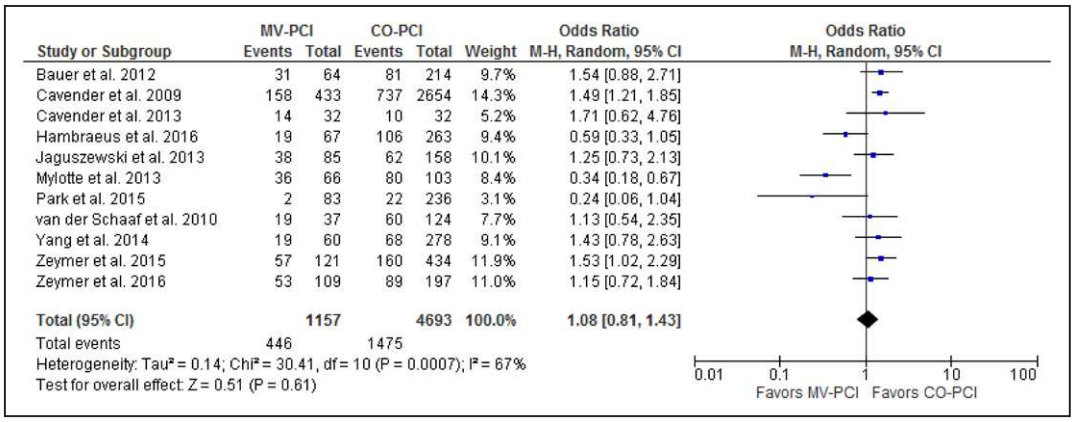

Figure 2. Comparison of short-term mortality after multivessel (MV) versus culprit vessel–only (CO) percutaneous coronary intervention (PCI). Studies included in this analysis are Bauer et al,[6] Cavender et al,[13] Cavender et al,[14] Hambraeus et al,[15] Jaguszewski et al,[16] Mylotte et al,[18] Park et al,[19] van der Schaaf et al,[20] Yang et al,[21] Zeymer et al,[1] and Zeymer et al.[22] CI indicates confidence interval.

(19.8%) underwent MV-PCI during the index catheterization. The proportion of patients undergoing MV-PCI in individual studies ranged from 14.0% to 39.1%. Baseline patient and procedural characteristics for the 2 groups in each study are summarized in Tables II and III in the Data Supplement.

Short-Term Mortality

All 11 studies provided data on the primary end point of short-term mortality. There was no statistically significant difference in short-term mortality with MV-PCI compared with CO-PCI (OR, 1.08; 95% CI, 0.81–1.43; *P*=0.61; I^2=67%; Figure 2). There was no evidence of publication bias (Figure IA in the Data Supplement).

Secondary End Points

Event rates at 6- and 12-month follow-up were used for analyses of secondary efficacy end points. The mean duration of follow-up weighted for the sample size was 9.8 months. There was no significant difference in long-term mortality (OR, 0.84; 95% CI, 0.54–1.30; *P*=0.43; I^2=64%) or cardiovascular death (OR, 0.72; 95% CI, 0.42–1.23; *P*=0.23; I^2=60%) between MV-PCI versus CO-PCI (Figures 3 and 4). Similarly, rates of reinfarction (OR, 1.65; 95% CI, 0.84–3.26; *P*=0.15; I^2=2%) and repeat revascularization (OR, 1.13; 95% CI, 0.76–1.69; *P*=0.54; I^2=0%) did not differ significantly between the 2 groups (Figures 5 and 6).

Analyses of safety end points revealed a nonsignificant trend toward more in-hospital stroke (OR, 1.64; 95% CI, 0.98–2.72; *P*=0.06; I^2=0%) and renal failure (OR, 1.30; 95% CI, 0.98–1.72; *P*=0.06; I^2=0%) with MV-PCI when compared with CO-PCI (Figure 7A and 7B). Major bleeding was also nonsignificantly higher with MV-PCI (OR, 1.47; 95% CI, 0.39–5.63; *P*=0.57; I^2=90%), but there was substantial heterogeneity likely due the different definitions of bleeding

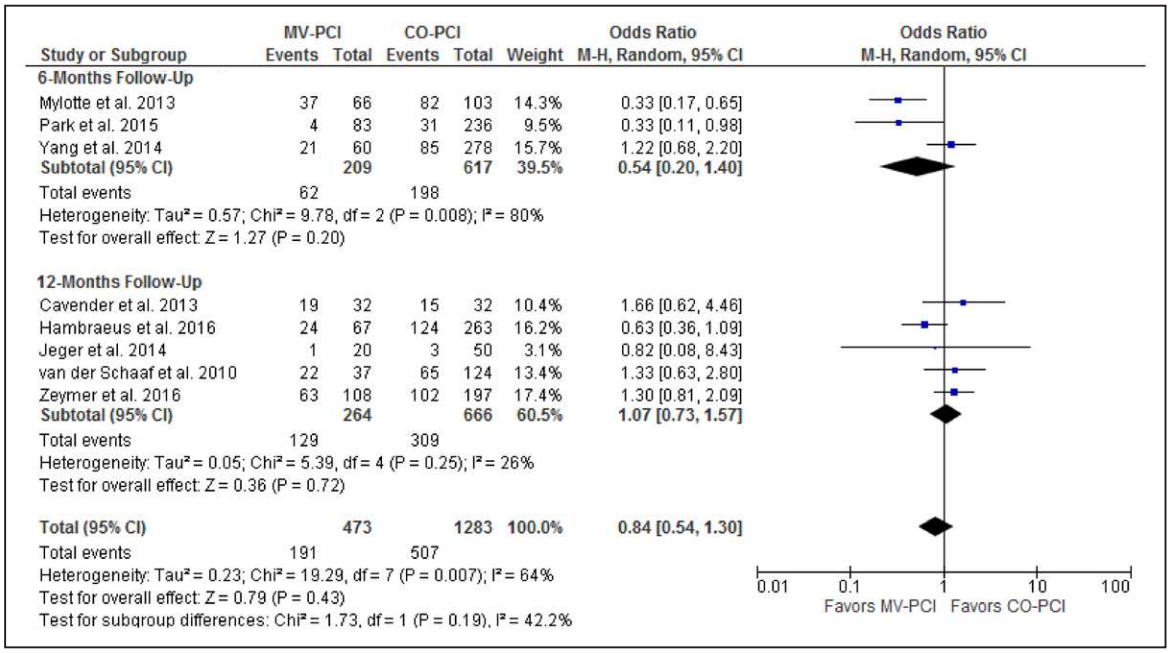

Figure 3. Comparison of long-term mortality after multivessel (MV) versus culprit vessel–only (CO) percutaneous coronary intervention (PCI). Studies included in this analysis are Cavender et al,[14] Hambraeus et al,[15] Jeger et al,[17] Mylotte et al,[18] Park et al,[19] van der Schaaf et al,[20] Yang et al,[21] and Zeymer et al.[22] CI indicates confidence interval.

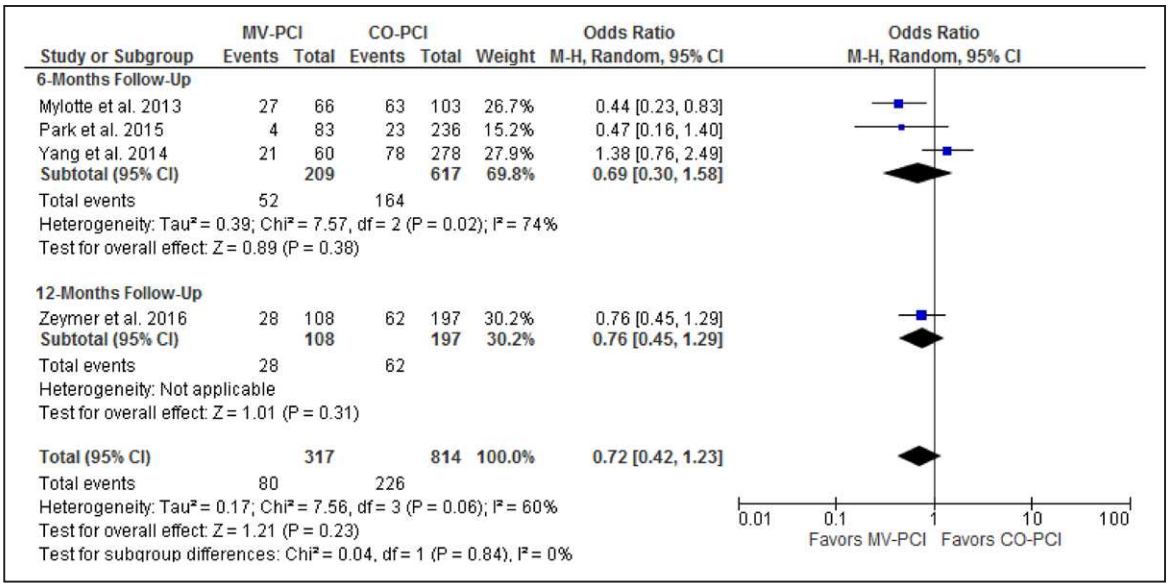

Figure 4. Comparison of cardiovascular death after multivessel (MV) versus culprit vessel–only (CO) percutaneous coronary intervention (PCI). Studies included in this analysis are Mylotte et al,[18] Park et al,[19] Yang et al,[21] and Zeymer et al.[22] CI indicates confidence interval.

used in different studies (Figure 7C). No publication bias was observed for any of the secondary end points (Figure IB through IH in the Data Supplement).

Sensitivity Analyses, Cumulative Meta-Analyses, and Meta-Regression

Sensitivity analyses after excluding single-center studies and studies with <50% drug-eluting stent use showed similar results for short- and long-term mortality (Table IV in the Data Supplement). Similarly, there was no significant difference in long-term mortality with MV-PCI versus CO-PCI after excluding studies with <1 year follow-up. Chronological cumulative meta-analyses did not reveal a time-dependent effect for most end points, except cardiovascular death (Figure II in the Data Supplement). MV-PCI was associated with significant reduction in cardiovascular death in an earlier study, but this effect became nonsignificant with the addition of studies that included data from more recent years. Meta-regression with multiple covariates (as mentioned before) showed no evidence of effect modification by any of the variables on the primary end point of short-term mortality (Figure III in the Data Supplement).

Discussion

In this meta-analysis of nonrandomized studies of patients with cardiogenic shock complicating STEMI, we found no significant difference in short-term mortality, long-term

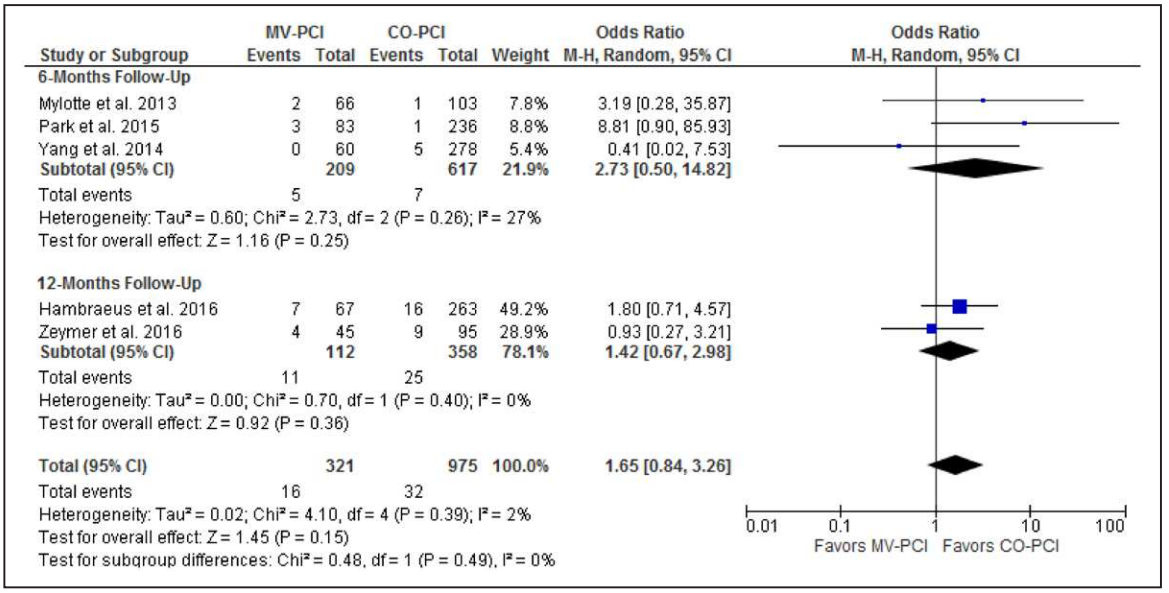

Figure 5. Comparison of reinfarction after multivessel (MV) versus culprit vessel–only (CO) percutaneous coronary intervention (PCI). Studies included in this analysis are Hambraeus et al,[15] Mylotte et al,[18] Park et al,[19] Yang et al,[21] and Zeymer et al.[22] CI indicates confidence interval.

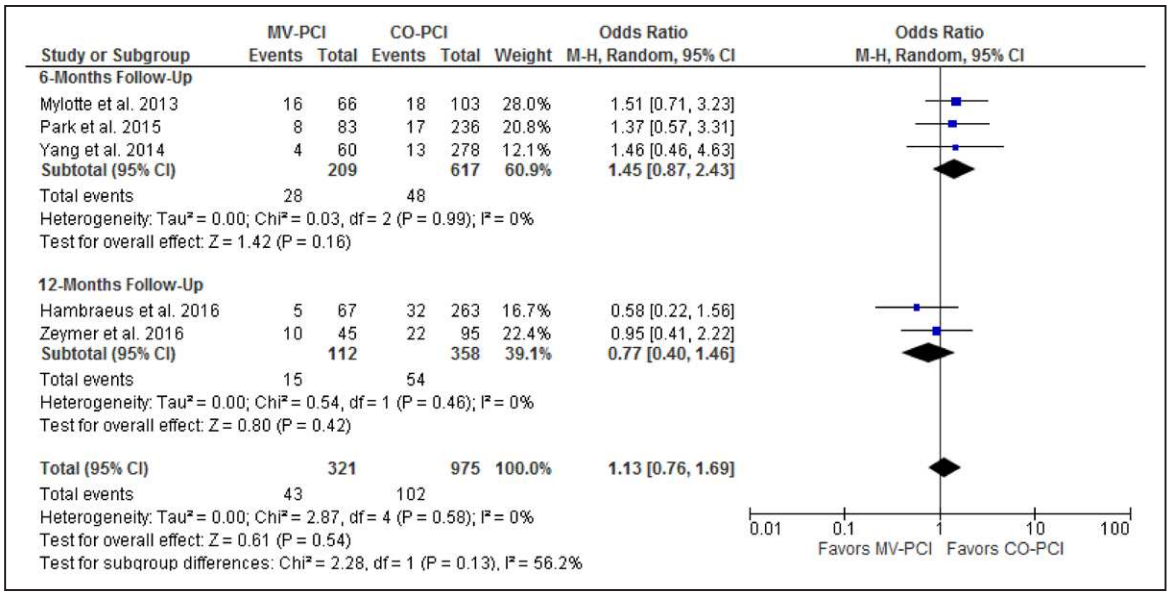

Figure 6. Comparison of repeat revascularization after multivessel (MV) versus culprit vessel–only (CO) percutaneous coronary intervention (PCI). Studies included in this analysis are Hambraeus et al,[15] Mylotte et al,[18] Park et al,[19] Yang et al,[21] and Zeymer et al.[22] CI indicates confidence interval.

mortality, cardiovascular death, reinfarction, or repeat revascularization with immediate/single-stage MV-PCI versus CO-PCI. There was a nonsignificant trend toward higher rates of in-hospital stroke and renal failure with MV-PCI compared with CO-PCI. To our knowledge, this is the first meta-analysis comparing MV-PCI versus CO-PCI specifically in patients with cardiogenic shock complicating STEMI.

The optimal revascularization strategy (MV-PCI versus CO-PCI) in patients with STEMI complicated by cardiogenic shock remains unknown. MV-PCI of nonculprit arteries may theoretically limit infarct size and preserve left ventricular function, both of which are associated with improved survival in patients with acute MI.[27,28] However, in our meta-analysis, immediate MV-PCI was not associated with reduction in short- or long-term mortality in patients with cardiogenic shock complicating STEMI, compared with CO-PCI. The lack of difference may be related to the imbalance in baseline characteristics in nonrandomized studies and the fact that we were unable to adjust for patient and operator characteristics which may have influenced the choice of revascularization strategy. Because all included studies were nonrandomized, it is possible that any potential benefit of MV-PCI was lost because patients who underwent MV-PCI were sicker and therefore did worse compared with those undergoing CO-PCI. Nonetheless, even in patients with STEMI without cardiogenic shock, the PRAMI (Preventive Angioplasty in Acute Myocardial Infarction) and CvLPRIT (Complete Versus Lesion-Only Primary PCI Pilot Study) trials showed no difference in all-cause mortality with immediate MV-PCI versus CO-PCI.[7,9] Similarly, previous pairwise and network meta-analyses of randomized and nonrandomized studies that included patients with STEMI with or without cardiogenic shock have also shown similar or higher all-cause mortality with single-stage MV-PCI versus CO-PCI, but lower short- and long-term mortality with staged MV-PCI compared with both CO-PCI and single-stage MV-PCI.[23,29] During our literature search for the current meta-analysis, we found 5 studies which included patients with or without cardiogenic shock undergoing single-stage MV-PCI or staged MV-PCI.[30–34] However, these studies included few patients and did not report outcomes separately in patients with cardiogenic shock and those undergoing staged MV-PCI.

RCTs and meta-analyses of RCTs in patients with STEMI without cardiogenic shock have shown a significant reduction in repeat revascularization and a nonsignificant trend toward reduced MI with MV-PCI when compared with CO-PCI.[7,35,36] However, in patients with STEMI with cardiogenic shock, we found no significant difference in reinfarction or repeat revascularization with MV-PCI versus CO-PCI. The end point of repeat revascularization is influenced by the fact that 100% of patients with MV-PCI undergo additional revascularization of the noninfarct-related arteries upfront. Successful MV-PCI may prevent early and late recurrent ischemia or infarction because of the noninfarct-related lesions. On the contrary, complicated or unsuccessful PCI of the noninfarct-related artery during MV-PCI may increase the risk of periprocedural MI because of distal embolization, side-branch occlusion, coronary dissection, no-reflow, or other procedure-related factors.[37] Some of the challenges interventionalists might encounter while performing PCI in STEMI patients with cardiogenic shock may include stent undersizing because of coronary vasospasm as a result of concomitant administration of catecholamines and increased risk of thrombotic complications because of poor coronary flow. Similarly, patient-related factors including MVD, reduced left ventricular ejection fraction, and presence of systemic inflammation, all of which are common in patients with cardiogenic shock, may also increase the risk of periprocedural MI.[37]

In patients with STEMI without cardiogenic shock, MV-PCI is not associated with an increased risk of stroke, contrast-induced nephropathy, or major bleeding.[7–9,35] On the contrary, we observed a nonsignificant trend toward higher rates of in-hospital stroke and renal failure with MV-PCI compared with CO-PCI in patients with cardiogenic shock complicating STEMI. Although presentation with STEMI, use of intra-aortic

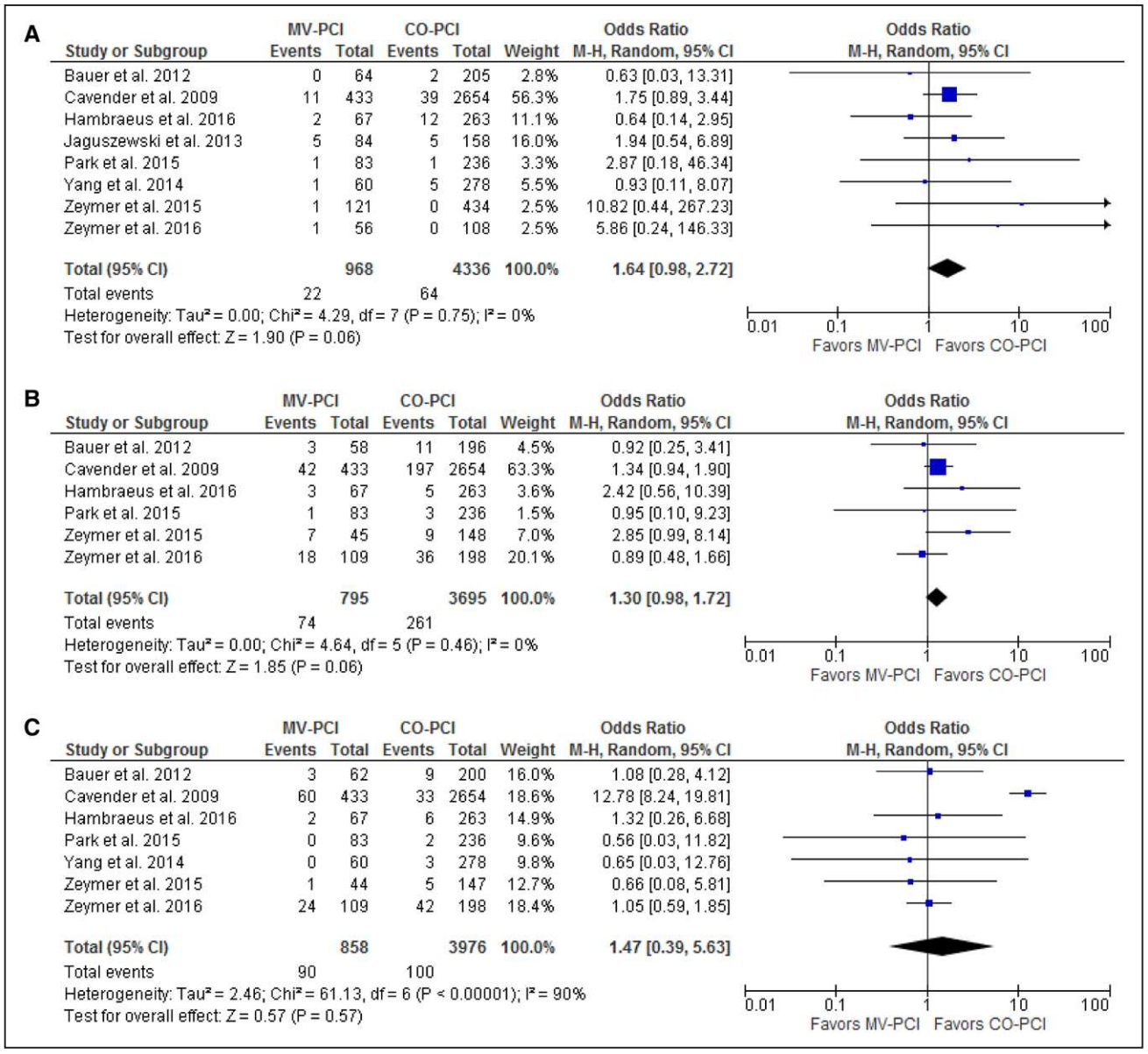

Figure 7. Comparison of in-hospital stroke (**A**), renal failure (**B**), and major bleeding (**C**) after multivessel (MV) versus culprit vessel–only (CO) percutaneous coronary intervention (PCI). Studies included in this analysis are Bauer et al,[6] Cavender et al,[13] Hambraeus et al,[15] Jaguszewski et al,[16] Park et al,[19] Yang et al,[21] Zeymer et al,[1] and Zeymer et al.[22] CI indicates confidence interval.

balloon pump, and use of greater contrast volumes are independent predictors of PCI-related stroke, MV-PCI is not independently associated with an increased risk of ischemic stroke.[38,39] The nonsignificant higher stroke rate with MV-PCI in our meta-analysis may be because of selection bias, with the potential that sicker patients were more likely to undergo MV-PCI. In addition, factors associated with PCI-related stroke such as longer procedure time and number of catheter exchanges were not evaluated. Further, it is difficult to diagnose stroke clinically in this patient population as many of them also had concomitant cardiac arrest and require mechanical ventilation necessitating sedation. Presentation with STEMI and cardiogenic shock is associated with 2- to 3-fold higher risk of developing acute kidney injury after PCI.[40] This together with the use of higher amounts of contrast during MV-PCI may explain the trend toward higher rates of renal failure in this patient population.

Limitations

Given the lack of RCTs, this meta-analysis included only nonrandomized studies and had all limitations of observational data including selection bias and unmeasured confounding. In the studies included, the choice of revascularization strategy was at the operator's discretion and was likely influenced by patient and operator characteristics for which we were unable to adjust because of the lack of patient-level data. For example, the exact stenosis severity was not known, and the majority of included studies defined MVD with a cutoff of ≥50% stenosis as opposed to ≥70%, meaning that a proportion of patients classified as MVD getting CO-PCI may in fact not have had another severe stenosis. This point is especially relevant, as after the SHOCK trial publication, many operators would have felt compelled to attempt complete revascularization in patients who truly had multiple severe stenoses. In addition, the influence of shock severity on

outcomes could not be determined.[41] Moderate-to-severe heterogeneity was seen for some of the end points studied. The degree of complete revascularization in the MV-PCI group was not known. Our meta-analysis addresses the question of single-stage MV-PCI versus CO-PCI but does not provide insights into staged MV-PCI as a revascularization strategy in patients with cardiogenic shock. As mentioned earlier, although we found 5 studies which included patients with or without cardiogenic shock who underwent single-stage or staged MV-PCI, none of these studies provided data separately in the subgroup of shock patients.[30–34] Nonetheless, it is difficult to compare CO-PCI versus staged MV-PCI in nonrandomized studies in this particular patient population without introducing substantial survival bias (sicker patients are likely to die while waiting for staged MV-PCI). Last, although this meta-analysis included 11 nonrandomized studies, 52.8% of the patients came from a single study.[13]

Conclusions

Notwithstanding the limitations of nonrandomized data, this carefully performed meta-analysis provides important evidence that in patients with cardiogenic shock complicating STEMI, immediate/single-stage MV-PCI may not provide additional benefit in improving short- or long-term mortality beyond that offered by successful PCI of the culprit vessel alone. Well-designed, adequately powered RCTs are needed to confirm or refute these findings and to determine the optimal revascularization strategy in this high-risk patient population. The ongoing COMPLETE (Complete versus Culprit-only Revascularization to Treat Multivessel Disease After Primary PCI for STEMI [NCT01740479]) and CULPRIT-SHOCK (Culprit Lesion Only PCI Versus Multivessel PCI in Cardiogenic Shock) trials will provide important answers.[42] The COMPLETE trial will determine whether a strategy of staged PCI of all suitable nonculprit lesions is superior to CO-PCI in reducing the composite outcome of cardiovascular death or MI in patients with MVD and STEMI. The CULPRIT-SHOCK trial will examine whether CO-PCI plus additional staged revascularization is superior to immediate/single-stage MV-PCI in reducing 30-day mortality and severe renal failure requiring renal replacement therapy in 706 acute MI (STEMI and non-STEMI) patients with cardiogenic shock and MVD.[42]

Disclosures

Dr Bhatt is in advisory board of Cardax, Elsevier Practice Update Cardiology, Medscape Cardiology, and Regado Biosciences; in board of directors of Boston VA Research Institute and Society of Cardiovascular Patient Care; in chair of American Heart Association Quality Oversight Committee; in data monitoring committees of Cleveland Clinic, Duke Clinical Research Institute, Harvard Clinical Research Institute, Mayo Clinic, Population Health Research Institute; receives honoraria from American College of Cardiology (Senior Associate Editor, Clinical Trials and News, ACC.org), Belvoir Publications (Editor in Chief, Harvard Heart Letter), Duke Clinical Research Institute (clinical trial steering committees), Harvard Clinical Research Institute (clinical trial steering committee), HMP Communications (Editor in Chief, Journal of Invasive Cardiology), Journal of the American College of Cardiology (Guest Editor; Associate Editor), Population Health Research Institute (clinical trial steering committee), Slack Publications (Chief Medical Editor, Cardiology Today's Intervention), Society of Cardiovascular Patient Care (Secretary/Treasurer), WebMD (CME steering committees); takes other roles in Clinical Cardiology (Deputy Editor), NCDR-ACTION Registry Steering Committee (Chair), and VA CART (Veterans Affairs Clinical Assessment Reporting and Tracking) Research and Publications Committee (Chair); receives research funding from Amarin, Amgen, AstraZeneca, Bristol-Myers Squibb, Eisai, Ethicon, Forest Laboratories, Ischemix, Lilly, Medtronic, Pfizer, Roche, Sanofi Aventis, and The Medicines Company; receives royalties from Elsevier (Editor, *Cardiovascular Intervention: A Companion to Braunwald's Heart Disease*); acts as a site co-investigator for Biotronik, Boston Scientific, and St. Jude Medical; acts as a trustee for American College of Cardiology; and receives unfunded research from FlowCo, PLx Pharma, and Takeda. Dr James reports institutional research grants from Astra Zeneca, The Medicines Company, Abbott Vascular, Boston Scientific, and Gilead; and honoraria form Astra Zeneca, and Boston Scientific. The other authors report no conflicts.

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Culprit Vessel–Only Versus Multivessel Percutaneous Coronary Intervention in Patients With Cardiogenic Shock Complicating ST-Segment–Elevation Myocardial Infarction: A Collaborative Meta-Analysis

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SUPPLEMENTAL MATERIAL

Supplemental Tables:

Table 1. Assessment of the Quality of Nonrandomized Studies Included in the Meta-Analysis Using the Newcastle-Ottawa Scale

Study	Selection	Comparability	Outcome
Bauer et al. 2012[1]	★★★★	★☆	★☆☆
Cavender et al. 2009[2]	★★★★	★★	★☆☆
Cavender et al. 2013[3]	★★★★	★★	★★★
Hambraeus et al. 2016[4]	★★★★	☆☆	★★★
Jaguszewski et al. 2013[5]	★★★★	☆☆	★★☆
Mylotte et al. 2013[6]	★★★★	★☆	★★★
Park et al. 2015[7]	★★★★	★★	★★★
van der Schaaf et al. 2010[8]	★★★★	★☆	★★★
Yang et al. 2014[9]	★★★★	★☆	★★★
Zeymer et al. 2015[10]	★★★★	★☆	★☆☆
Zeymer et al. 2016[11]	★★★★	★☆	★★★

Table 2. Baseline Patient and Procedural Characteristics from Nonrandomized Studies Included in the Meta-Analysis Stratified According to the Revascularization Strategy

	Bauer 2012[1]		Cavender 2009[2]		Cavender 2013[3]		Hambraeus 2016[4]		Jaguszewski 2013[5]		Mylotte 2013[6]	
	EHS-PCI		ACC-NCDR		Single Center		SCAAR		AMIS Plus		French Multicenter	
	MV-PCI	CO-PCI	MV-PCI	CO-PCI	MV-PCI	CO-PCI	MV-PCI	CO-PCI	MV-PCI	CO-PCI	MV-PCI	CO-PCI
n	**64**	**214**	**433**	**2,654**	**32**	**32**	**67**	**263**	**85**	**158**	**66**	**103**
Age, years	66.7 ± 12.0	65.0 ± 12.5	64.4 ± 13.0	66.3 ± 12.8	64 ± 14	64 ± 15	68.2 ± 11.8	71.3 ± 10.9	64.7 ± 11.7	65.0 ± 11.2	65.0 ± 12.4	68.5 ± 11.8
Female	28.1	32.2	35.8	35.3	31	25	32.8	34.6	22.4	25.3	34.0	28.2
BMI, kg/m^2	27.2 ± 4.5	27.4 ± 4.3	27.9 ± 4.5	27.1 ± 4.9	29 ± 7	27 ± 10					25.1 ± 2.7	27.0 ± 7.5
Smoking	57.7	52.7	56.1	62.1	66	72	49.3	41.9	57.1	54.5	34.8	31.1
Dyslipidemia	38.5	52.0	50.6	50.7			22.4	16.7	39.7	57.9	45.5	40.8
HTN	57.9	65.0	59.8	63.4	72	69	38.8	39.5	56.5	61.1	53.0	48.5
DM	37.3	31.6	30.5	27.3	34	22	26.9	23.6	26.1	25.0	25.8	25.2
Prior MI	30.0	33.2	22.2	23.1	31	31	9.0	10.6			21.2	30.1
Prior PCI	8.3	11.9	15.7	15.6	9	6	9.0	9.9	11.8	18.5	16.7	22.3
Prior CABG	0	0	5.1	10.1	9	9	0	0	3.9	6.2	6.1	4.9
HF	8.3	8.3	41.8	31.7			6.0	5.3	2.9	9.0		
Stroke	10.0	7.8	11.6	11.8	9	13	7.5	8.0	5.9	9.7		
PAD	5.0	9.3	8.8	11.3								
CKD	6.7	6.2	7.6	8.2	16	6	1.5	3.0	8.8	6.0		
Cardiac arrest	46.8	49.5							48.2	52.5	100	100
LVEF					23 ± 9	27 ± 10					31.0 ± 9.6	30.3 ± 9.0
>50%	11.4	11.9					7.5	10.3				
41-50%	8.6	12.7					9.0	13.7				
31-40%	34.3	29.9					13.4	14.4				
<30%	45.7	45.5	26.1	19.1			9.0	14.8	36.5	26.6		
Access site												
Femoral	95.3	97.2										
Brachial	0.0	0.5										
Radial	4.7	2.3										

No. of stenosed vessels												
2	40.6	45.8	54.7	55.9	56	38	74.6	48.3			48.5	52.4
3	59.4	54.2	45.3	44.1	44	18	25.4	51.3			51.5	47.6
Culprit vessel												
LM					3	9					21.2	7.8
LAD			49.4	36.8	50	50					47.0	43.7
CX			21.5	13.7	25	25					16.7	15.5
RCA			27.7	49.0	22	16					15.2	30.1
Bypass graft			2.1	5.5	0	0					0	2.9
Stent	89.1	84.6	84.5	97.9			100	94.7	92.2	88.0	98.5	93.2
DES	39.1	22.4	64.7	69.4			19.4	8.4	58.2	60.3		
No. of stents	1.8 ± 1.1	1.1 ± 0.7	1.1 ± 0.8	1.4 ± 0.7			2.6 ± 1.8	1.9 ± 1.2			2.6 ± 1.1	1.6 ± 0.9
Thrombectomy	17.2	16.7									39.4	39.8
IABP	34.4	24.0	66.3	52.8	67	65	50.7	46.4	65.1	46.5	76.3	
Inotropes	68.9	66.3										
Aspirin	85.2	83.4	83.2	82.3							100	100
Ticlopidine	3.3	0.5	0.2	0.5								
Clopidogrel	62.3	61.4	51.5	54.1							100	100
Prasugrel												
Ticagrelor												
UFH	77.0	71.9	81.4	83.0							100	100
LMWH	14.8	17.6	13.3	10.7								
Fondaparinux												
Bivalirudin	1.6	0.5	11.8	10.5								
GPI	54.1	53.3	79.5	79.7								
Procedural							100	100			80.3	75.7

success												
TIMI 3	62.9	71.9	82.9	89.4					87.3	85.6	81.9	77.7
Stenosis <30-50%	68.8	86.3	89.6	96.8							97.0	91.3

Categorical variables are presented as percentages and continuous variables as mean ± standard deviation.

HTN = hypertension, DM = diabetes mellitus, MI = myocardial infarction, PCI = percutaneous coronary intervention, CABG = coronary artery bypass grafting, HF = heart failure, PAD = peripheral artery disease, CKD = chronic kidney disease, LVEF = left ventricular ejection fraction, LM = left main, LAD = left anterior descending coronary artery, CX = circumflex coronary artery, RCA = right coronary artery, DES = drug-eluting stent, IABP = intra-aortic balloon pump, UFH = unfractionated heparin, LMWH = low-molecular weight heparin, GPI = glycoprotein IIb/IIIa inhibitor, TIMI = thrombolysis in myocardial infarction, MV-PCI = multivessel PCI, CO-PCI = culprit vessel-only PCI, EHS-PCI = Euro Heart Survey PCI Registry, ACC-NCDR = American College of Cardiology- National Cardiovascular Data Registry, SCAAR = Swedish Coronary Angiography and Angioplasty Registry, AMIS Plus = Acute Myocardial Infarction in Switzerland Plus Registry.

Table 3. Baseline Patient and Procedural Characteristics from Nonrandomized Studies Included in the Meta-Analysis Stratified According to the Revascularization Strategy

	Park 2015[7]		**Van der Schaaf 2010**[8]		**Yang 2014**[9]		**Zeymer 2015**[10]		**Zeymer 2016**[11]	
	KAMIR		**Single Center**		**KAMIR, KWGMI**		**ALKK-PCI**		**IABP-SHOCK II**	
	MV-PCI	**CO-PCI**	**MV-PCI**	**CO-PCI**	**MV-PCI**	**CO-PCI**	**MV-PCI**	**CO-PCI**	**MV-PCI**	**CO-PCI**
n	**83**	**236**	**37**	**124**	**60**	**278**	**121**	**434**	**109**	**197**
Age, years	65.3 ± 14.8	67.3 ± 14.1	67.0 ± 13.3	67.4 ± 11.4	66.1 ± 14.6	69.5 ± 13.3	66.5 ± 11.9	68.4 ± 12.1	69.8 ± 12.6	68.0 ± 14.8
Female	29	34.2	18.9	32.3	36.7	42.1	24.0	29.5	29.4	29.3
BMI, kg/m^2	24.0 ± 3.0	23.3 ± 3.7					27.6 ± 4.6	27.4 ± 4.4	26.4 ± 3.6	28.1 ± 3.7
Smoking	47.6	46.6	29.7	29.8	40.0	35.6	35.7	40.5	24.1	40.2
Dyslipidemia	9.8	9.7	24.3	24.2	21.7	23.4	73.0	71.5	40.2	37.8
HTN	53.7	54.5	29.7	25.8	50.0	57.9	80.5	77.5	65.7	71.4
DM	25.6	23.3	24.3	21.8	16.5	21.7	36.5	36.8	35.8	28.1
Prior MI					8.3	4.7	27.7	44.1	13.8	26.8
Prior PCI			18.9	8.1	3.3	6.1	13.3	18.7	11.1	24.2
Prior CABG			5.4	9.7	0	1.4	0	0	2.8	4.5
HF										
Stroke							18.5	5.1	11.9	6.6
PAD							20.3	18.0	11.9	10.1
CKD							50.0	37.2	20.4	18.7
Cardiac arrest	3.3	4.2			11.7	16.9	18.2	13.6	44.0	42.9
LVEF	49.8 ± 15.6	50.3 ± 11.1			48.5 ± 15.3	45.9 ± 13.9			34.6 ± 13.7	35.0 ± 14.8
>50%							4.5	14.9		
41-50%							22.7	17.5		
31-40%					38.4	34.1	19.7	19.3		
<30%							53.0	48.2		
Access site										
Femoral							92.6	97.5		
Brachial							1.7	0.5		
Radial							5.8	2.1		

No. of stenosed vessels										
2	48.4	56.7	37.8	46.8	53.3	55.8	31.3	37.4	31.2	44.4
3	46.0	39.9	62.2	53.2	46.7	44.2	68.7	62.6	68.8	55.6
Culprit vessel										
LM	2.4	0.8	0.0	5.6	0	0			14.7	6.6
LAD	31.5	25.9	56.8	43.5	40.0	38.8			47.7	43.4
CX	16.1	7.5	16.2	18.5	5.0	8.6			14.7	17.2
RCA	49.2	65.8	27.0	32.3	55.0	52.5			22.9	29.3
Bypass graft	0	0	0	0	0	0			0.0	3.0
Stent	100	100	70.3	61.3	96.7	94.2	90.9	85.7	97.2	91.9
DES	83.1	82.4			88.3	83.1	23.4	15.5	48.1	39.0
No. of stents	2.38 ± 1.09	1.32 ± 0.60			2.31 ± 1.09	1.41 ± 0.67				
Thrombectomy					31.7	27.7	14.7	10.3	72.5	68.2
IABP	18.5	16.3	73.0	61.3	33.3	25.9	33.0	28.2	47.7	53.5
Inotropes					81.7	81.7	59.3	56.5	95.4	89.4
Aspirin					100	100	98.2	94.5	87.0	93.4
Ticlopidine										
Clopidogrel					100	100	82.9	78.7	61.1	71.2
Prasugrel							0	4.1	19.4	21.7
Ticagrelor							0	0.8	7.8	5.3
UFH							91.5	95.8	90.7	94.4
LMWH							1.7	2.6	1.9	2.5
Fondaparinux							0	0.5		
Bivalirudin							4.0	2.4	19.4	9.6
GPI					18.3	25.2	61.2	62.5	54.6	52.5
Procedural success	96.8	95.1	94.6	80.2						

TIMI 3	90.7	88.0	73.0	68.5	80.0	84.2	67.8	74.7	80.7	77.3
Stenosis <30-50%										

Categorical variables are presented as percentages and continuous variables as mean ± standard deviation.

HTN = hypertension, DM = diabetes mellitus, MI = myocardial infarction, PCI = percutaneous coronary intervention, CABG = coronary artery bypass grafting, HF = heart failure, PAD = peripheral artery disease, CKD = chronic kidney disease, LVEF = left ventricular ejection fraction, LM = left main, LAD = left anterior descending coronary artery, CX = circumflex coronary artery, RCA = right coronary artery, DES = drug-eluting stent, IABP = intra-aortic balloon pump, UFH = unfractionated heparin, LMWH = low-molecular weight heparin, GPI = glycoprotein IIb/IIIa inhibitor, TIMI = thrombolysis in myocardial infarction, MV-PCI = multivessel PCI, CO-PCI = culprit vessel-only PCI, KAMIR = Korean Acute Myocardial Infarction Registry, KWGMI = Korea Working Group on Myocardial Infarction registry, ALKK-PCI = Arbeitsgemeinschaft Leitende Kardiologische Krankenhausärzte-PCI registry, IABP-SHOCK II = Intra-Aortic Balloon Pump in Cardiogenic Shock II.

Table 4. Sensitivity Analyses Results for Short- and Long-Term Mortality

	Short-Term Mortality	Long-Term Mortality
All Studies	1.08 (0.81-1.43) $P = 0.61$, $I^2 = 67\%$	0.79 (0.51-1.20) $P = 0.20$, $I^2 = 60\%$
Excluding Single-Center Studies	1.03 (0.75-1.43) $P = 0.84$, $I^2 = 73\%$	0.70 (0.41-1.19) $P = 0.19$, $I^2 = 69\%$
Excluding Studies With <50% DES Use	1.27 (0.86-1.86) $P = 0.23$, $I^2 = 51\%$	0.73 (0.28-1.92) $P = 0.53$, $I^2 = 55\%$
Excluding Studies With <1 Year Follow-Up	—	1.07 (0.73-1.57) $P = 0.72$, $I^2 = 26\%$

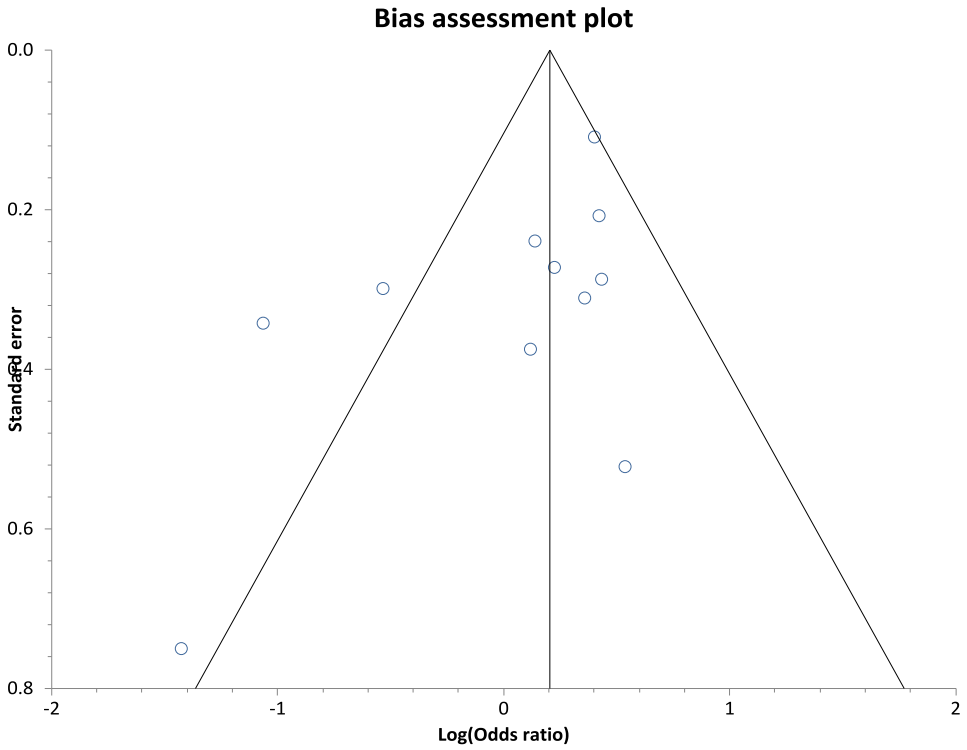
Estimates are odds ratios (95% confidence interval) using random-effect models.

DES = drug-eluting stent

Supplemental Figures and Figure Legends:

Figure 1. Publication Bias Assessment

A) Short-Term Mortality

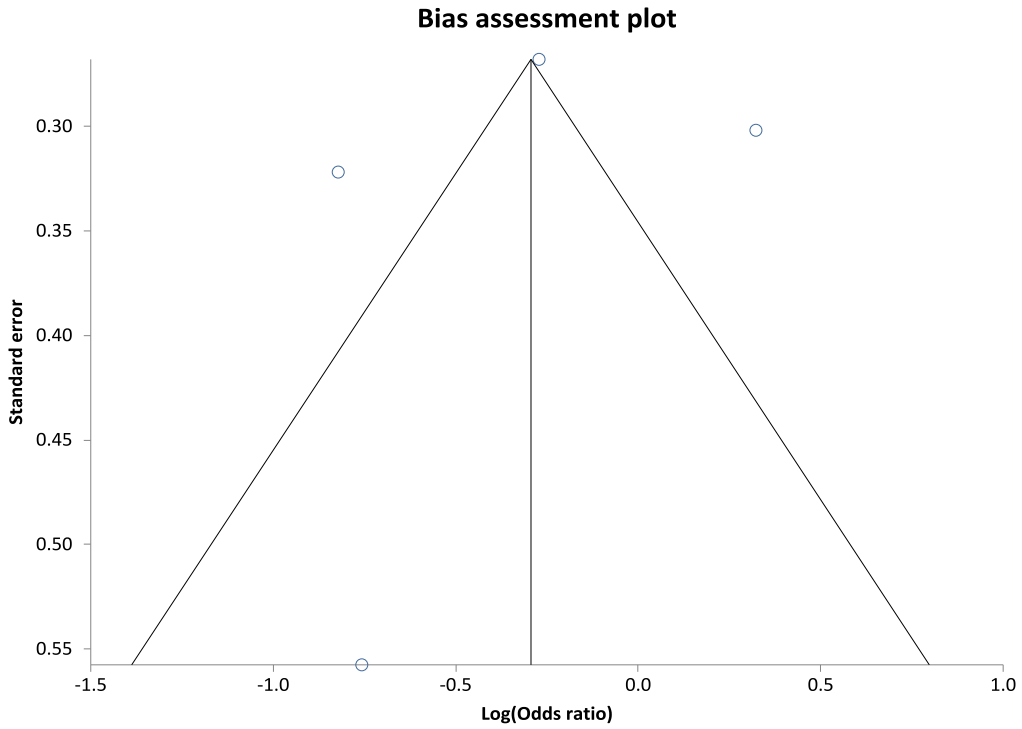


Bias indicators
Begg-Mazumdar: Kendall's tau = -0.381818 P = 0.0866
Egger: bias = -1.985231 (95% CI = -4.198118 to 0.227655) P = 0.073
Harbord-Egger: bias = -2.170399 (92.5% CI = -4.44215 to 0.101351) P = 0.0867

B) Long-Term Mortality

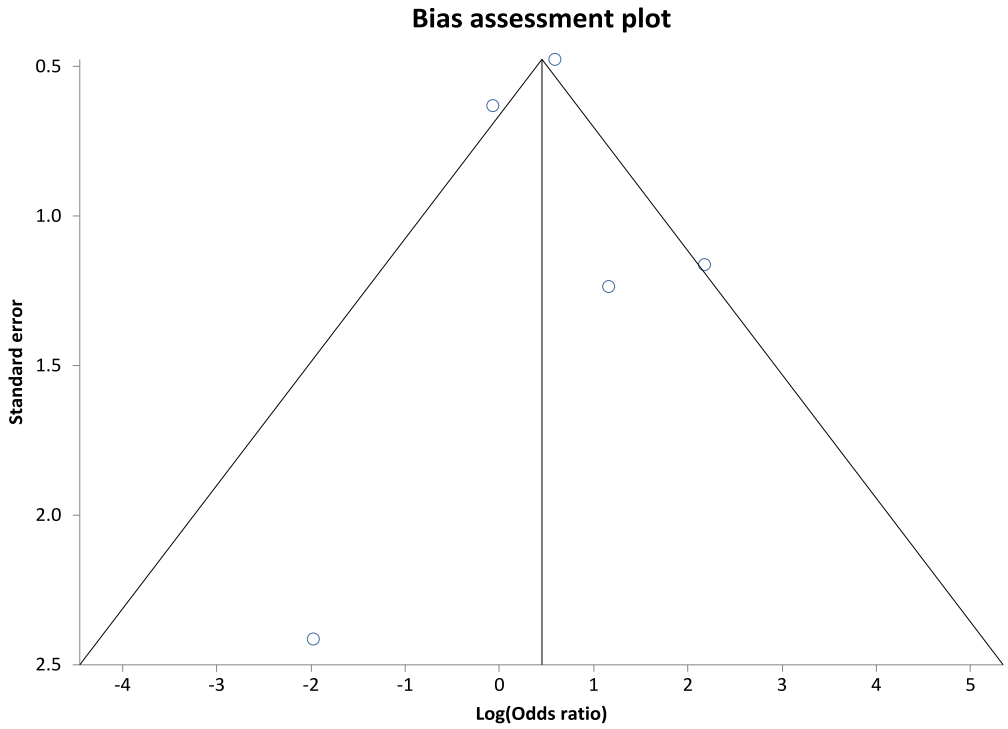
Bias indicators
Begg-Mazumdar: Kendall's tau = -0.357143 P = 0.1789 (low power)
Egger: bias = -1.237415 (95% CI = -5.210013 to 2.735183) P = 0.4748
Harbord-Egger: bias = -0.95809 (92.5% CI = -4.802415 to 2.886236) P = 0.6112

C) Cardiovascular Death



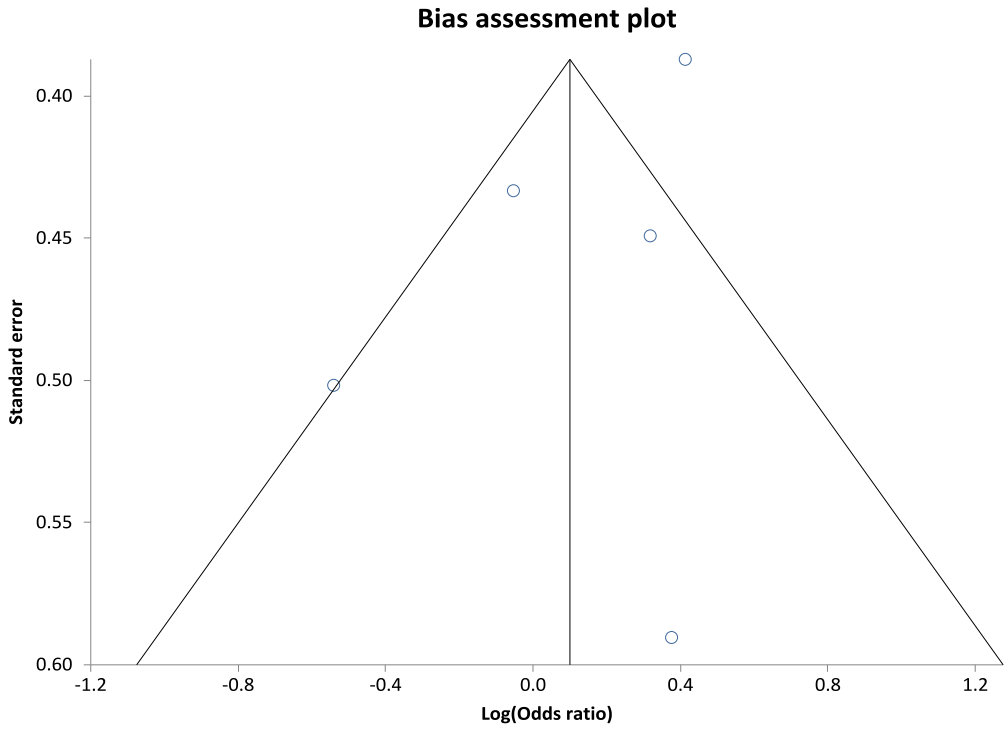
Bias indicators
Begg-Mazumdar: Kendall's tau = -0.333333 P = 0.3333 (low power)
Egger: bias = -2.250715 (95% CI = -18.606172 to 14.104742) P = 0.6138
Harbord-Egger: bias = -1.986646 (92.5% CI = -19.05863 to 15.085339) P = 0.7274

Reinfarction



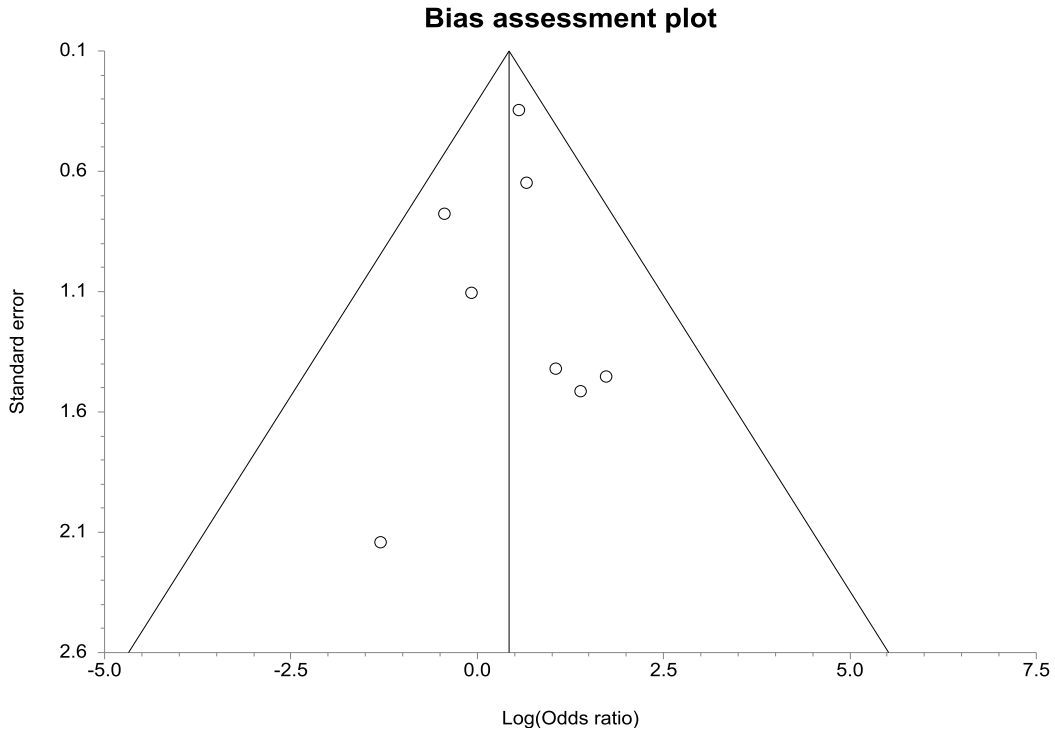
Bias indicators
Begg-Mazumdar: Kendall's tau = 0 P = 0.8167 (low power)
Egger: bias = 0.086448 (95% CI = -3.559767 to 3.732662) P = 0.9446
Harbord-Egger: bias = 0.847732 (92.5% CI = -4.359263 to 6.054727) P = 0.692

Repeat Revascularization



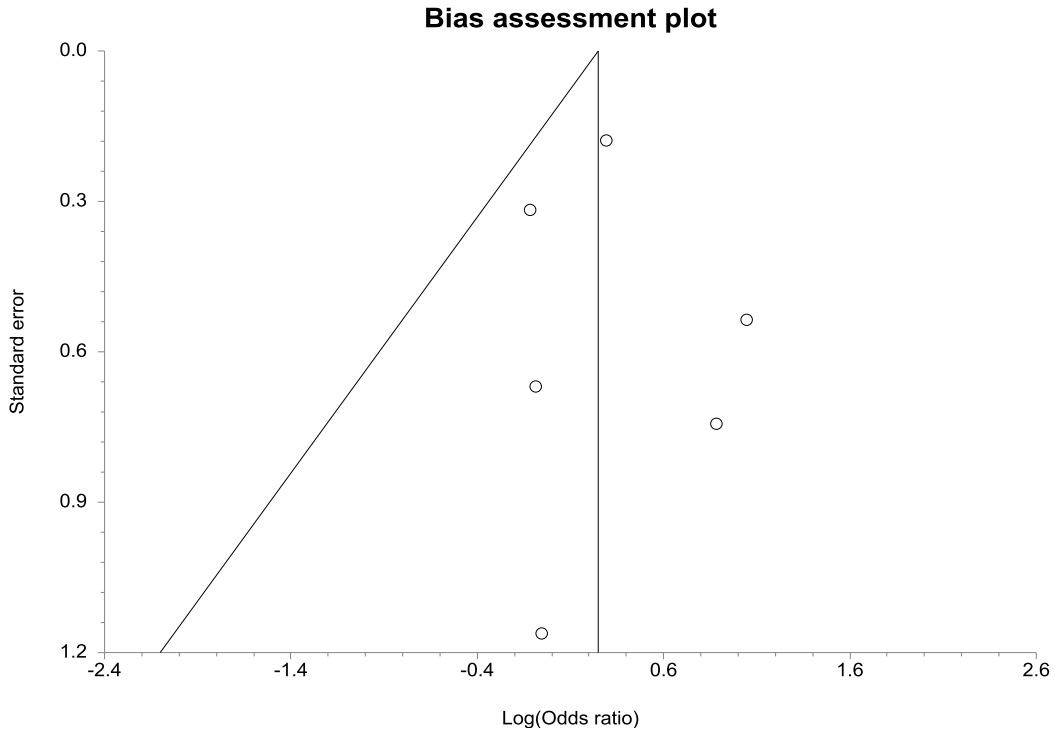
Bias indicators
Begg-Mazumdar: Kendall's tau = -0.4 P = 0.2333 (low power)
Egger: bias = -1.495805 (95% CI = -11.191538 to 8.199929) P = 0.6571
Harbord-Egger: bias = 1.012926 (92.5% CI = -6.51552 to 8.541371) P = 0.7422

Stroke



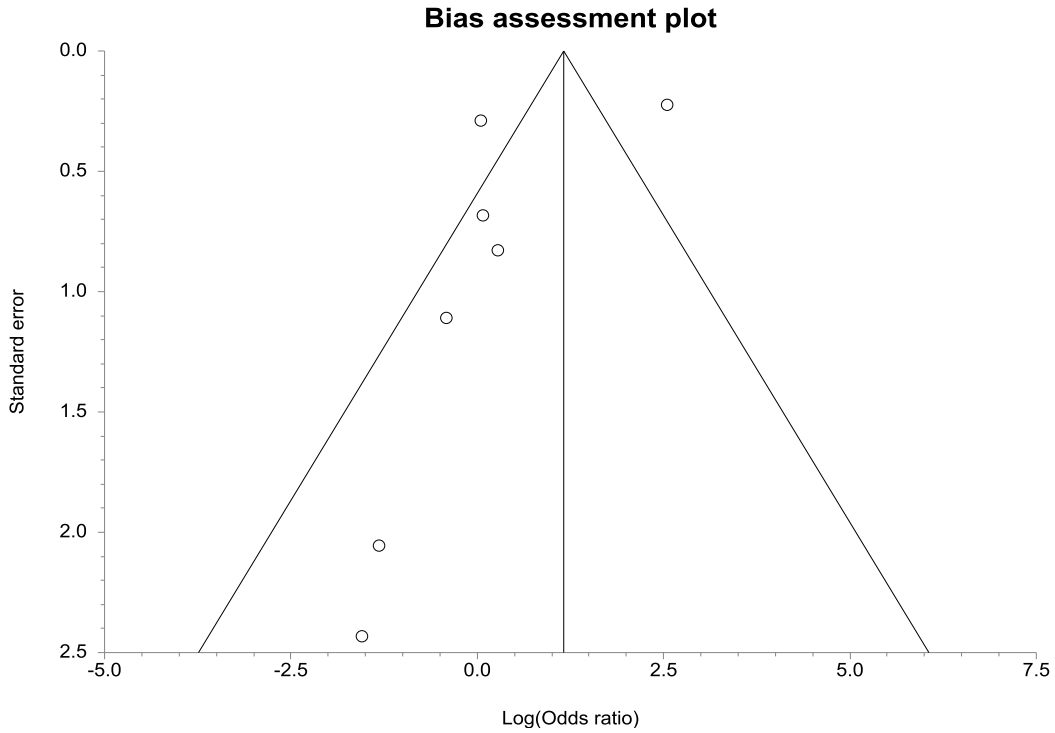
Bias indicators
Begg-Mazumdar: Kendall's tau = 0.142857 P = 0.7195 (low power)
Egger: bias = -0.061316 (95% CI = -1.315704 to 1.193072) P = 0.9087
Harbord-Egger: bias = 0.15828 (92.5% CI = -1.29748 to 1.61404) P = 0.8229

D) Renal Failure



Bias indicators
Begg-Mazumdar: Kendall's tau = 0.066667 P > 0.9999 (low power)
Egger: bias = 0.253726 (95% CI = -1.905845 to 2.413298) P = 0.7606
Harbord-Egger: bias = 0.398065 (92.5% CI = -1.573735 to 2.369865) P = 0.6544

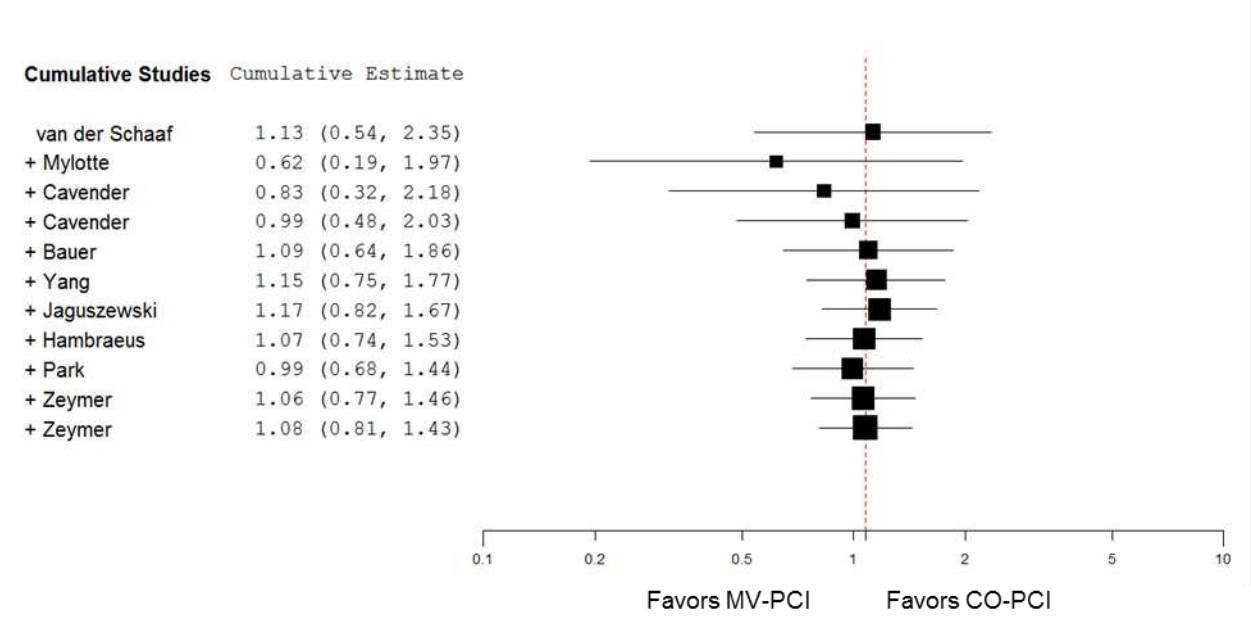
E) Major Bleeding



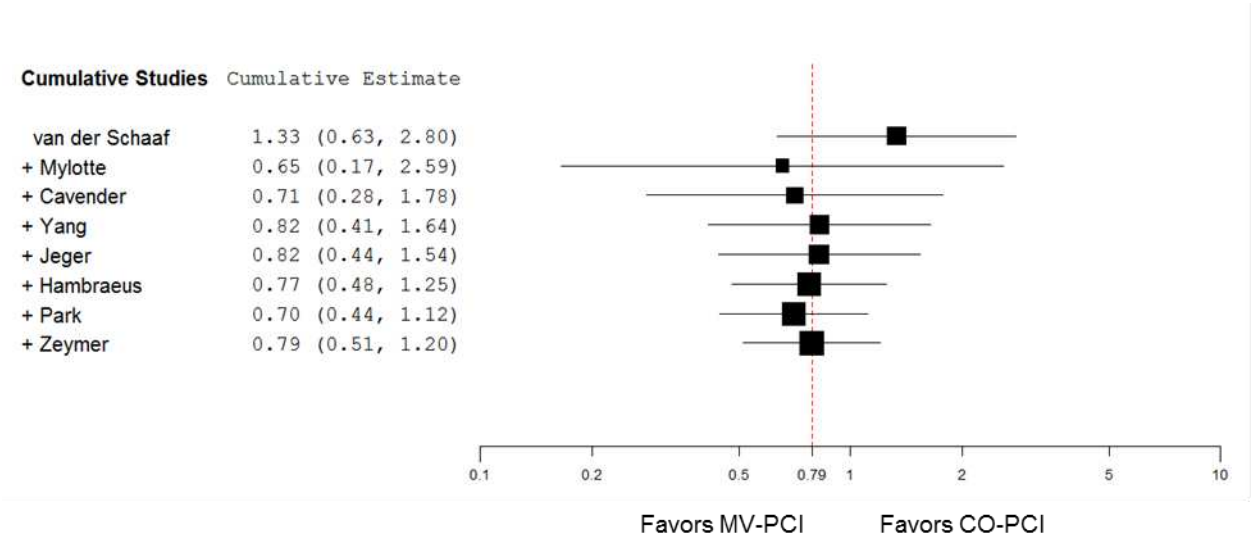
Bias indicators
Begg-Mazumdar: Kendall's tau = 0.333333 P = 0.3813 (low power)
Egger: bias = -2.449104 (95% CI = -6.9277 to 2.029493) P = 0.2188
Harbord-Egger: bias = -3.158874 (92.5% CI = -10.406249 to 4.0885) P = 0.3733

Figure 2. Chronological Cumulative Meta-Analysis

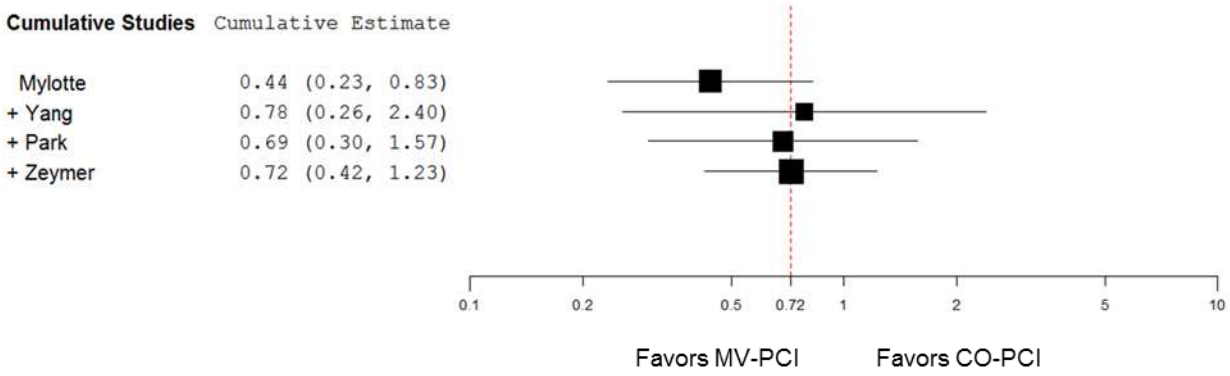
A) Short-Term Mortality



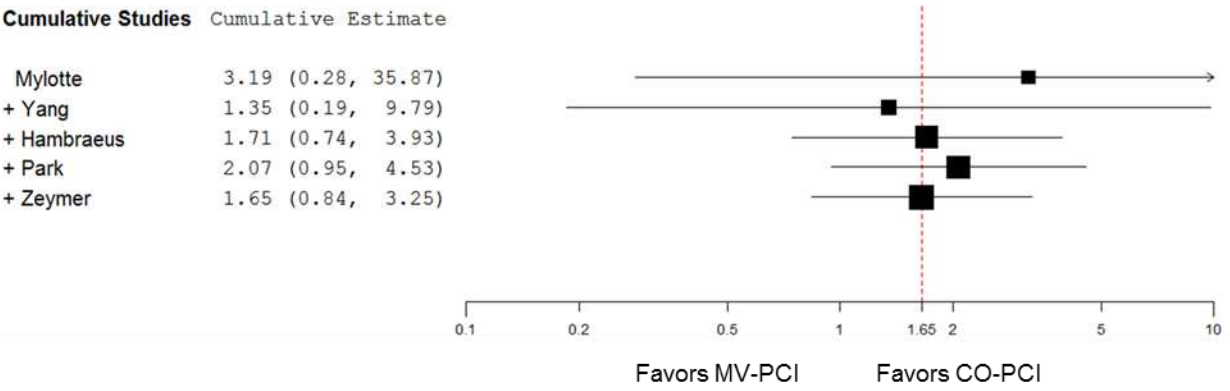
B) Long-Term Mortality



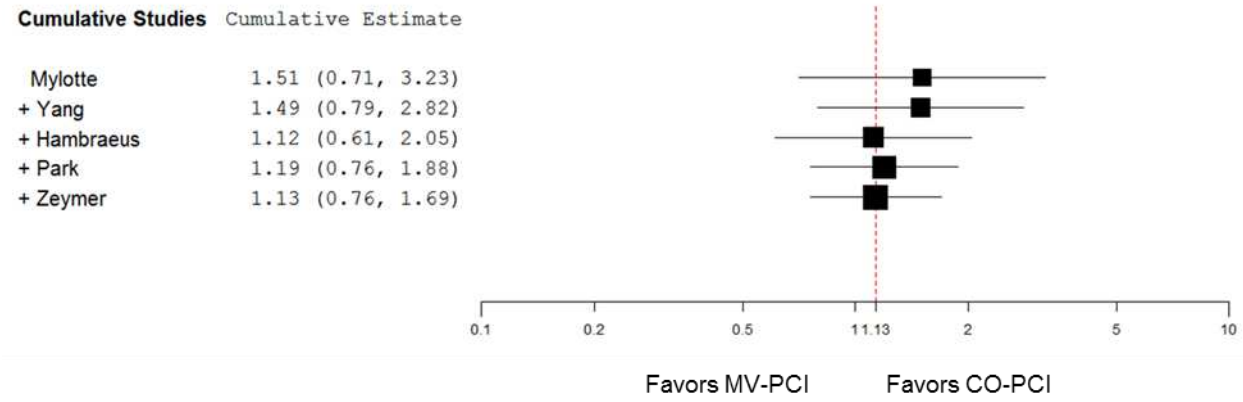
C) Cardiovascular Death



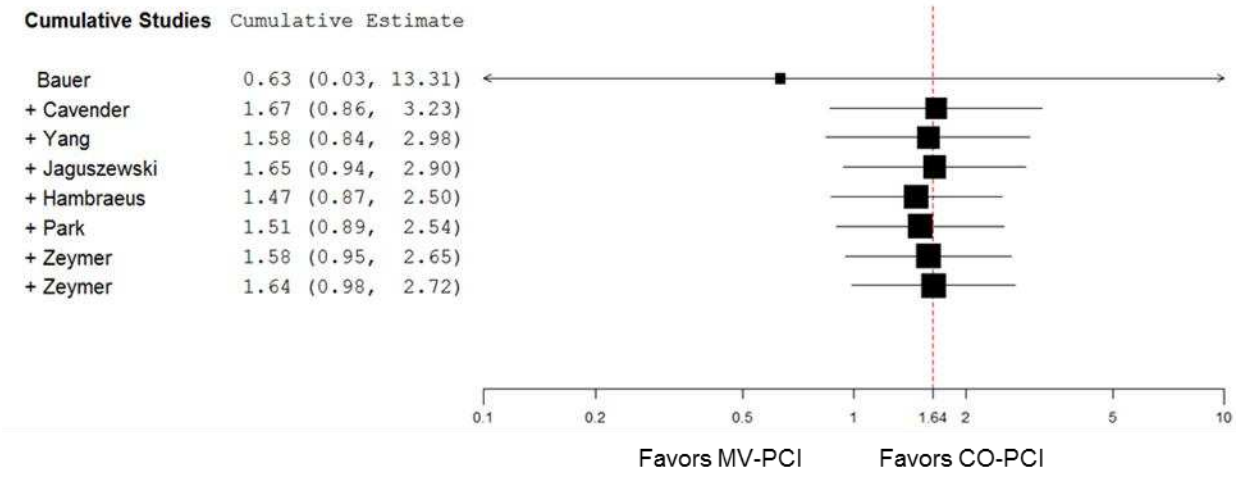
D) Reinfarction



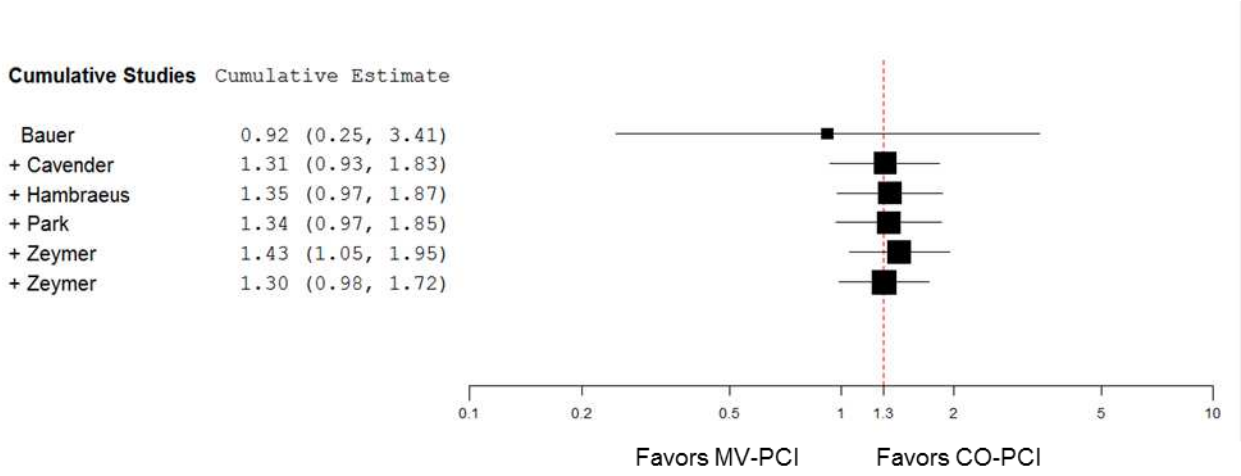
E) Repeat Revascularization



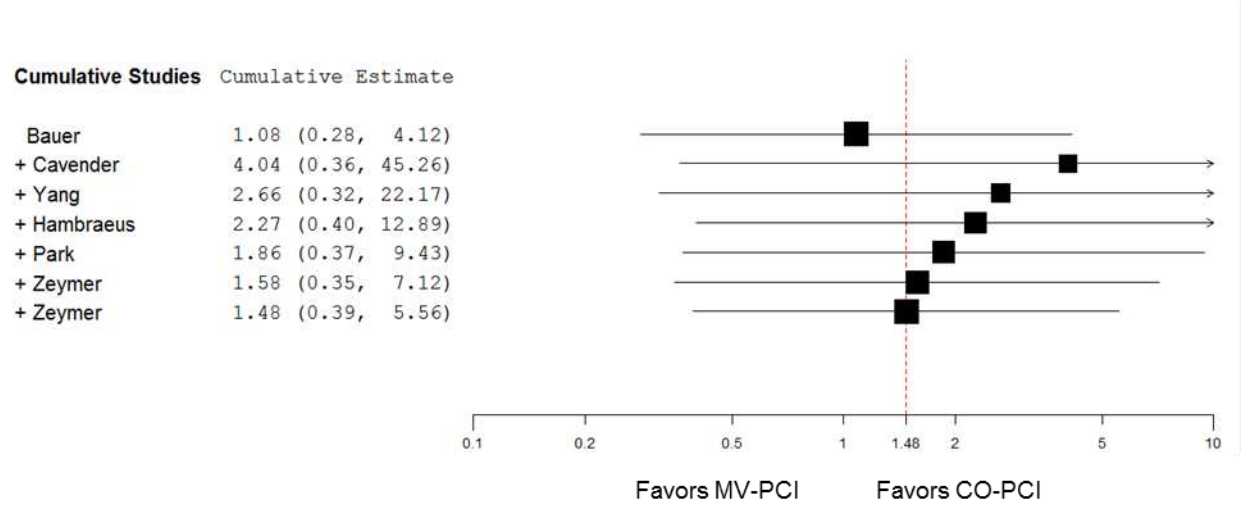
F) Stroke



G) Renal Failure



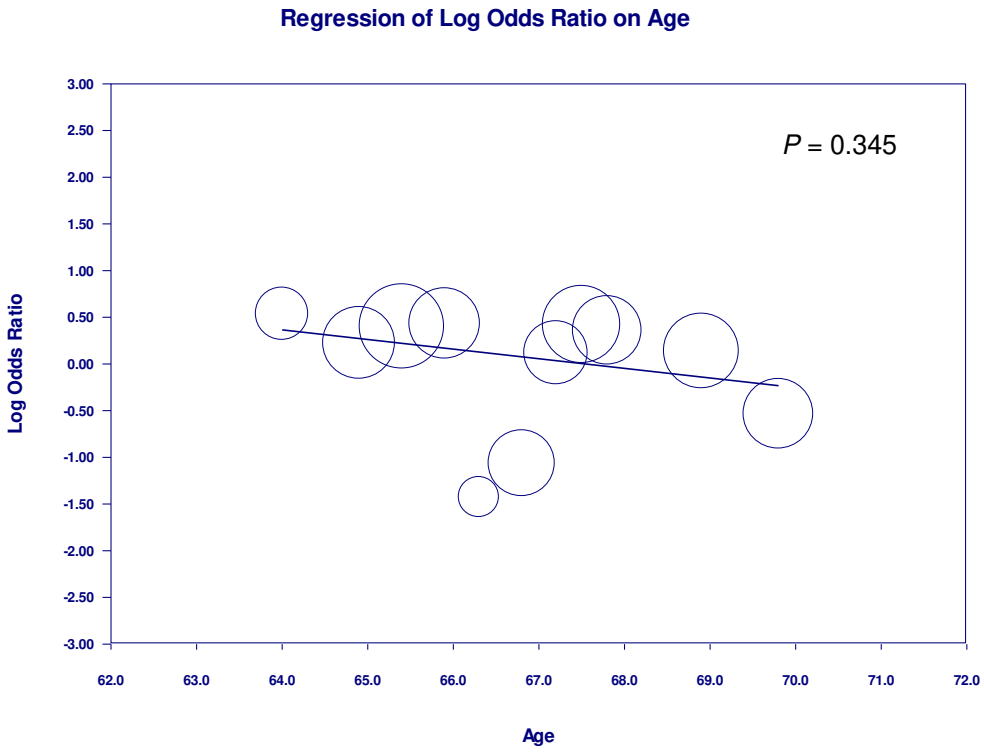
H) Major Bleeding



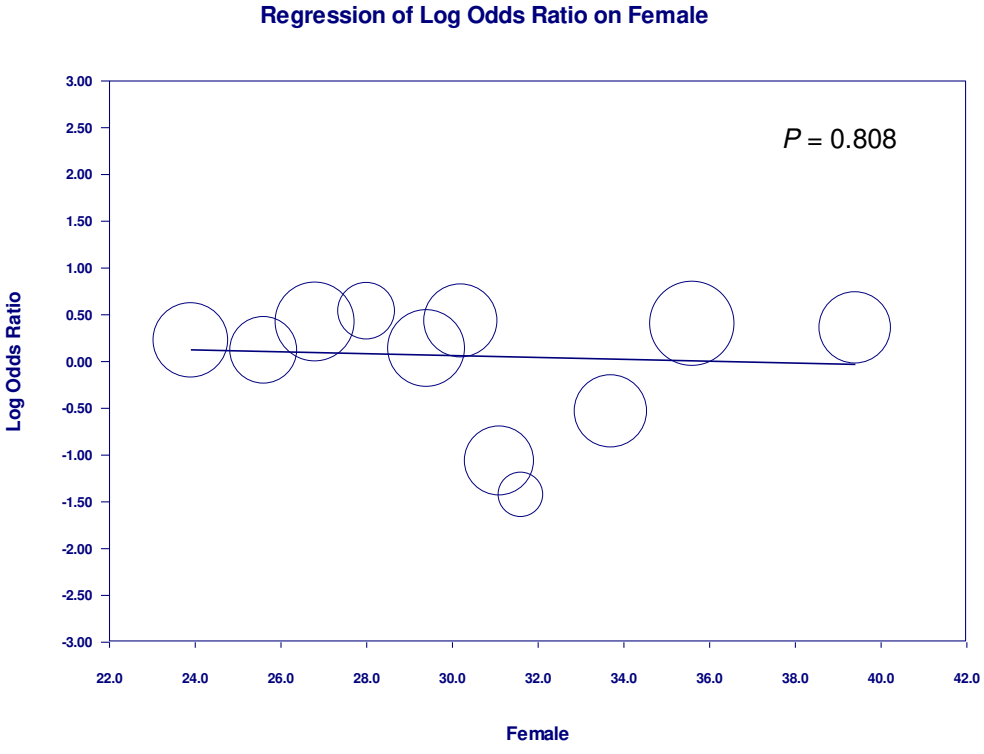
Studies included in these analyses are Bauer et al. 2012,[1] Cavender et al. 2009,[2] Cavender et al. 2014,[3] Hambraeus et al. 2016,[4] Jaguszewski et al. 2013,[5] Mylotte et al. 2013,[6] Park et al. 2015,[7] van der Schaaf et al. 2010,[8] Yang et al. 2014,[9] Zymer et al. 2015,[10] and Zeymer et al. 2016.[11]

Figure 3. Meta-Regression for Short-Term Mortality

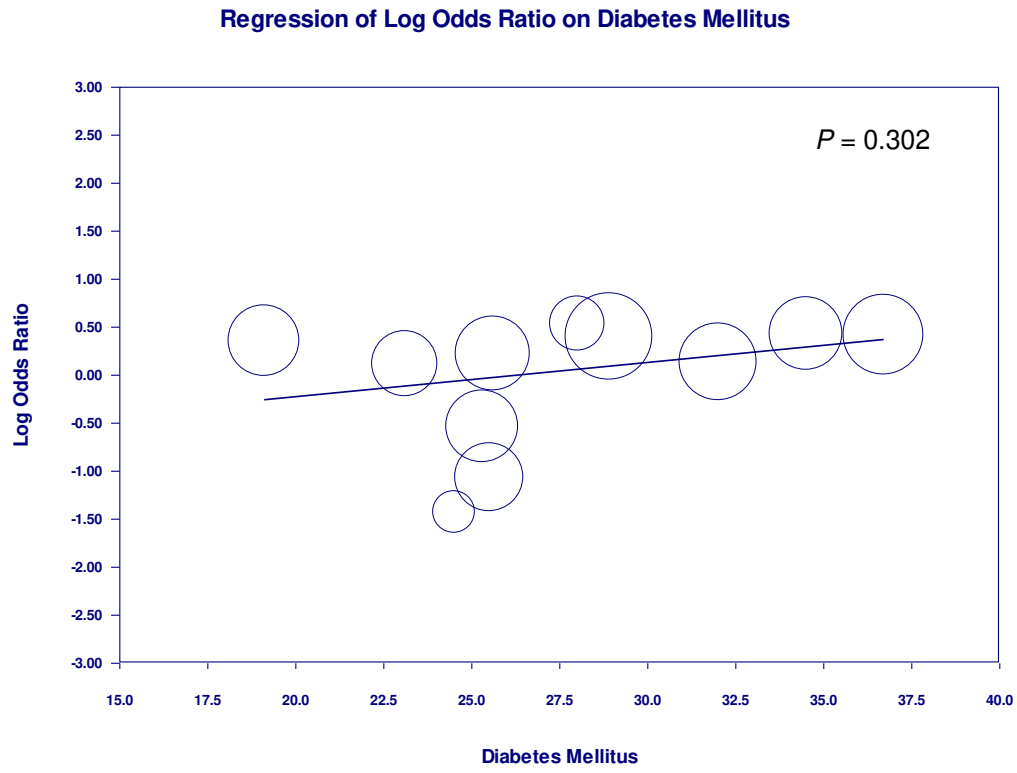
A)



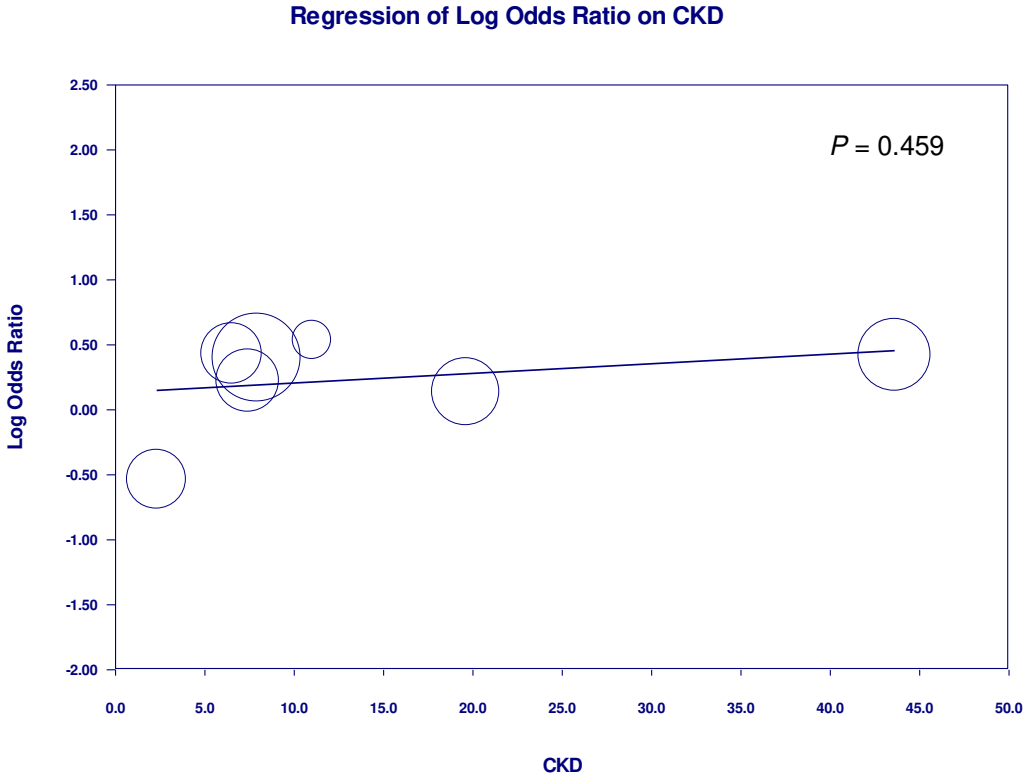
B)



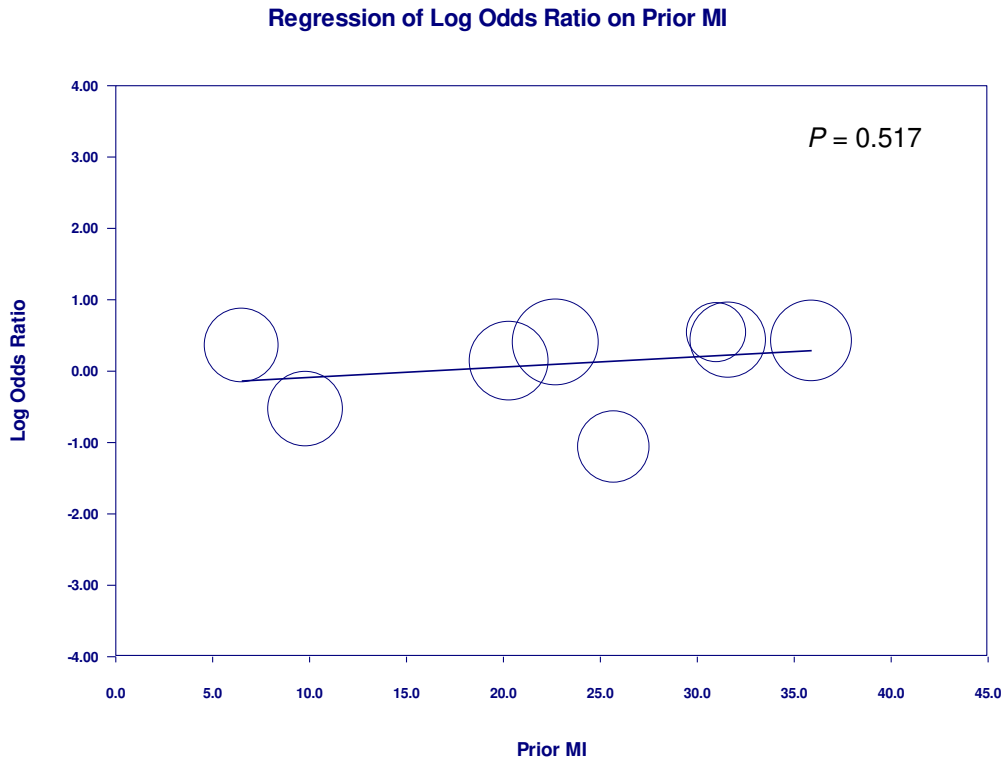
C)


Regression of Log Odds Ratio on Diabetes Mellitus
P = 0.302
Log Odds Ratio
3.00
2.50
2.00
1.50
1.00
0.50
0.00
-0.50
-1.00
-1.50
-2.00
-2.50
-3.00
15.0
17.5
20.0
22.5
25.0
27.5
30.0
32.5
35.0
37.5
40.0
Diabetes Mellitus

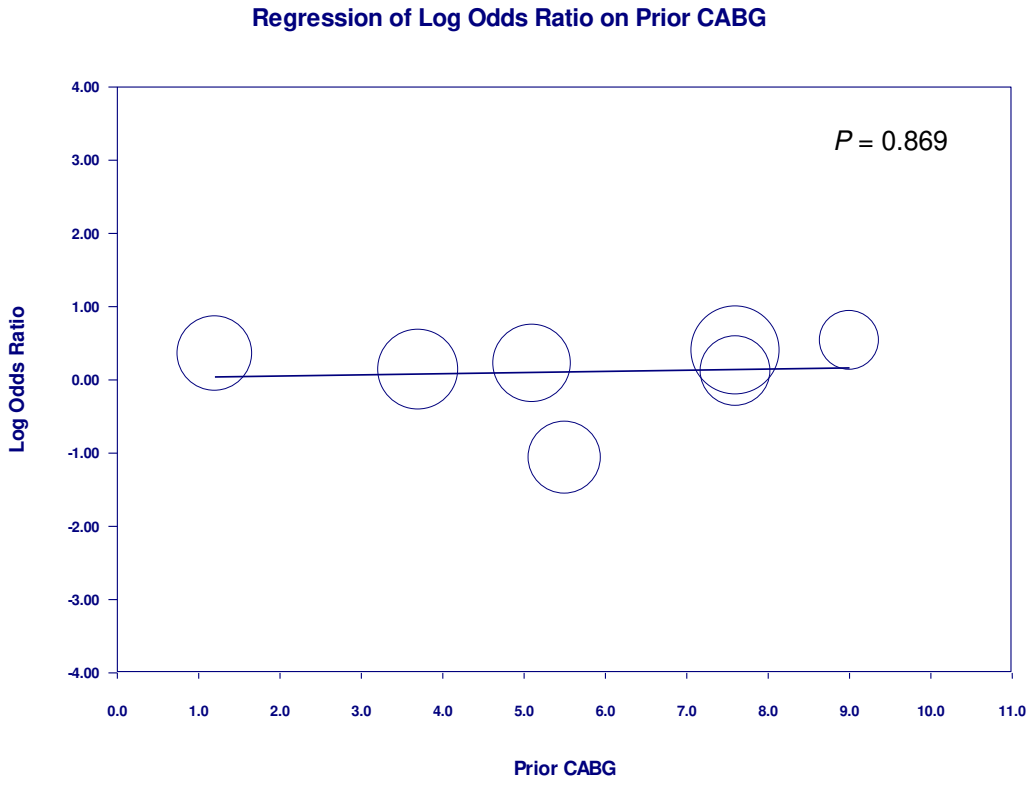
D)


Regression of Log Odds Ratio on CKD
P = 0.459
Log Odds Ratio
2.50
2.00
1.50
1.00
0.50
0.00
-0.50
-1.00
-1.50
-2.00
0.0
5.0
10.0
15.0
20.0
25.0
30.0
35.0
40.0
45.0
50.0
CKD

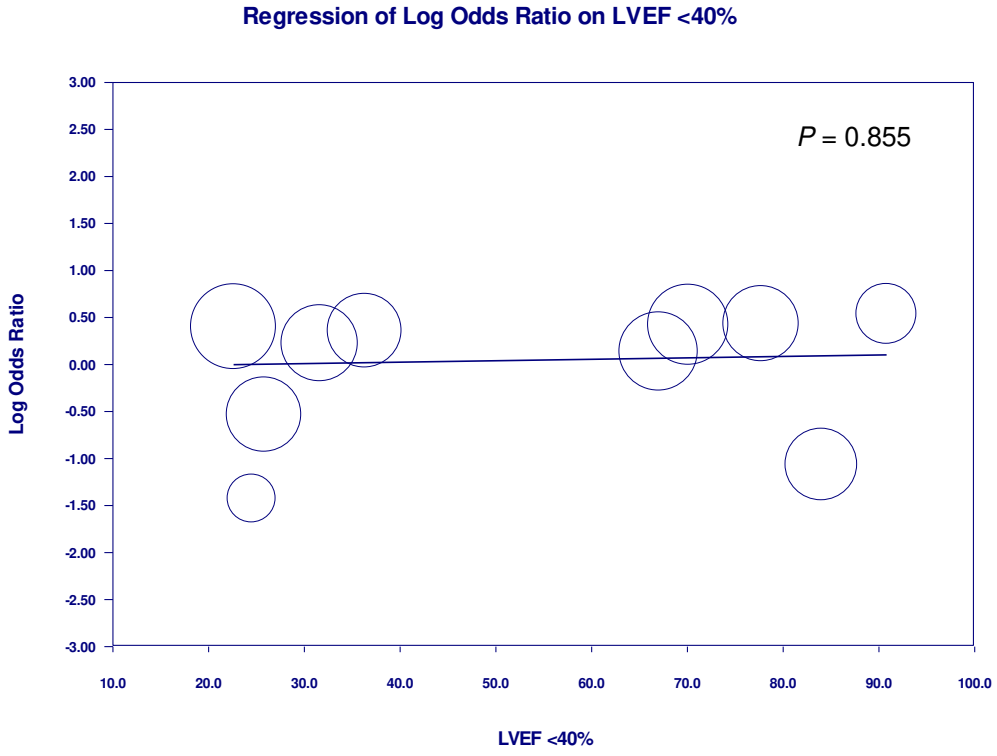
E)


Regression of Log Odds Ratio on Prior MI
P = 0.517
Log Odds Ratio
4.00
3.00
2.00
1.00
0.00
-1.00
-2.00
-3.00
-4.00
0.0
5.0
10.0
15.0
20.0
25.0
30.0
35.0
40.0
45.0
Prior MI

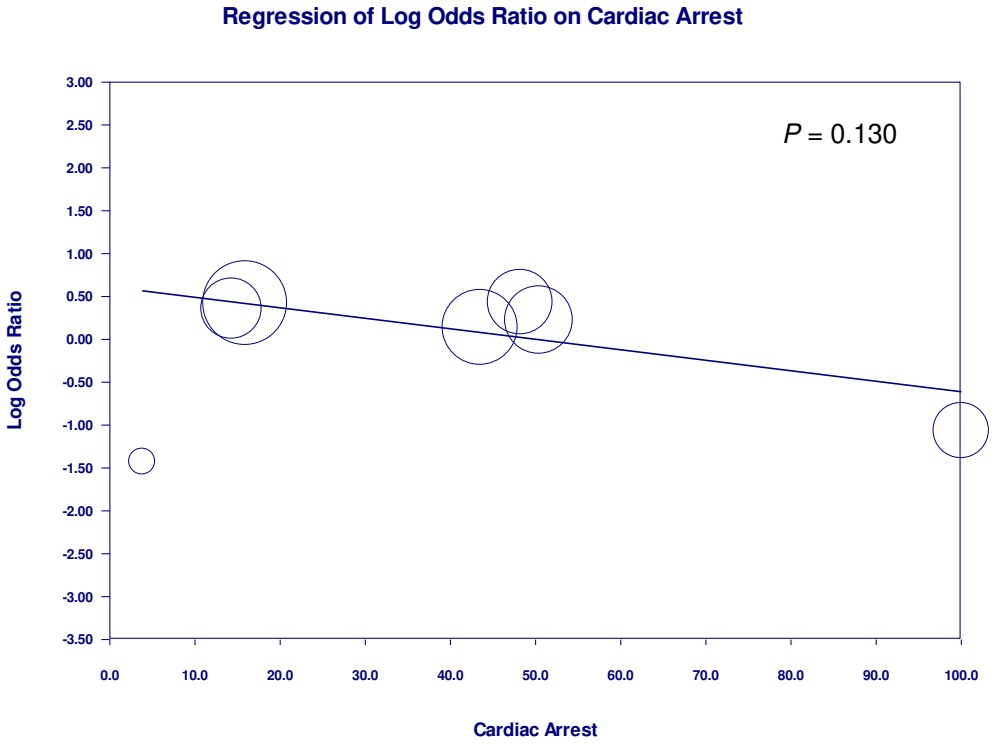
F)


Regression of Log Odds Ratio on Prior CABG
P = 0.869
Log Odds Ratio
4.00
3.00
2.00
1.00
0.00
-1.00
-2.00
-3.00
-4.00
0.0
1.0
2.0
3.0
4.0
5.0
6.0
7.0
8.0
9.0
10.0
11.0
Prior CABG

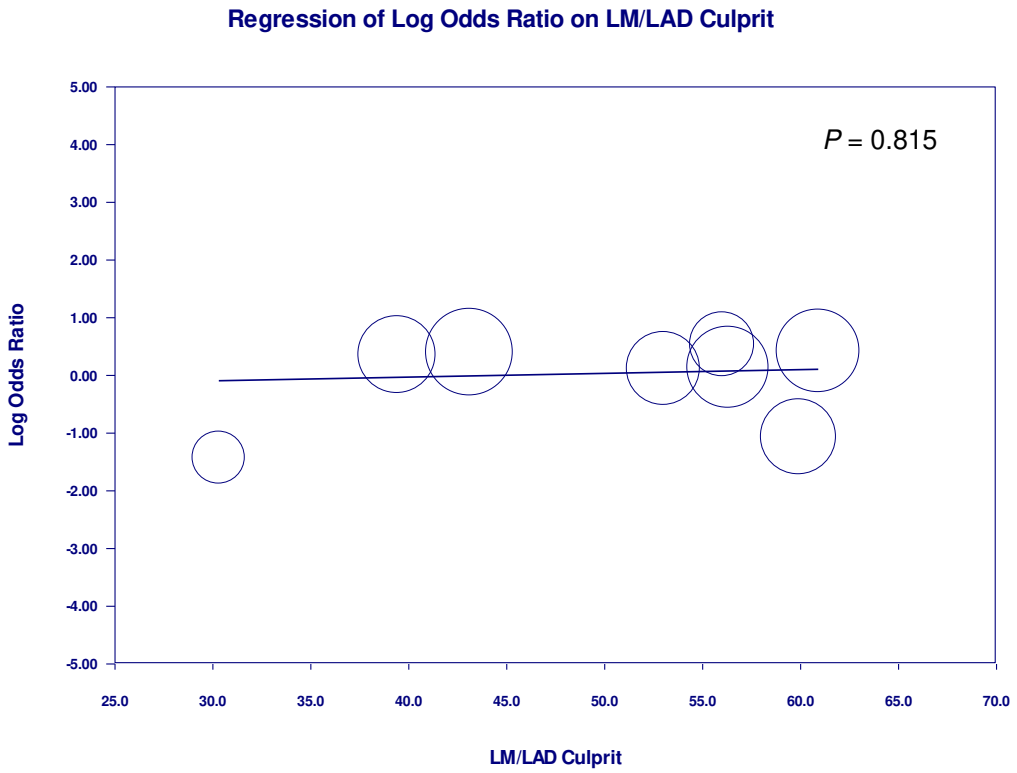
G)


Regression of Log Odds Ratio on LVEF <40%
P = 0.855
Log Odds Ratio
3.00
2.50
2.00
1.50
1.00
0.50
0.00
-0.50
-1.00
-1.50
-2.00
-2.50
-3.00
10.0
20.0
30.0
40.0
50.0
60.0
70.0
80.0
90.0
100.0
LVEF <40%

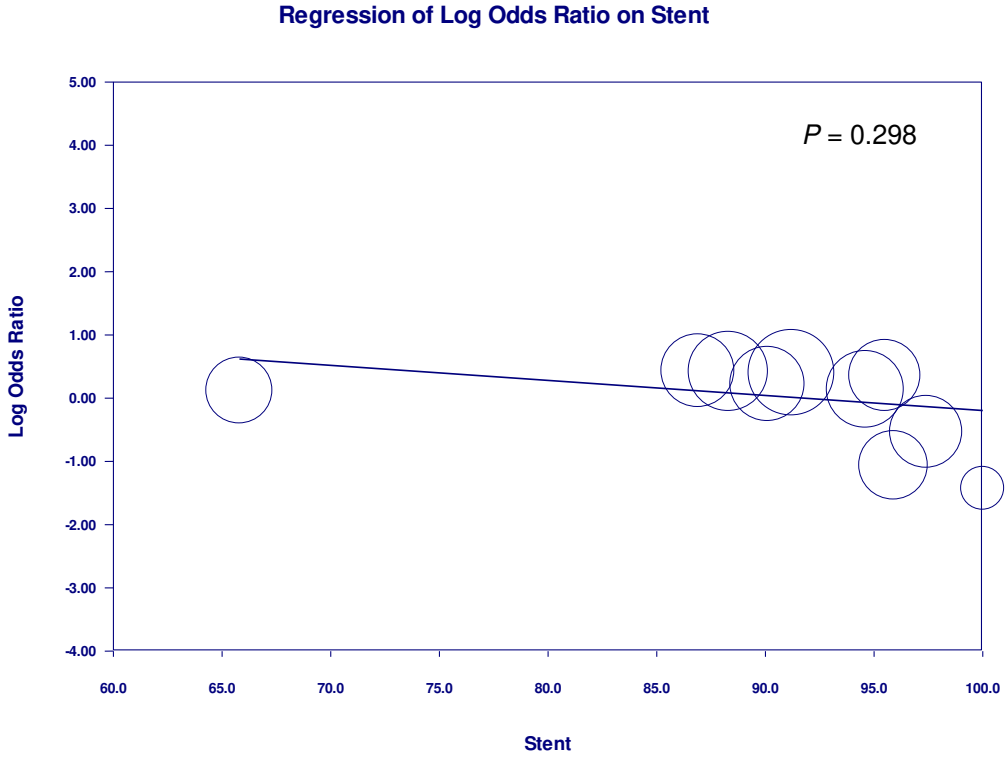
H)


Regression of Log Odds Ratio on Cardiac Arrest
P = 0.130
Log Odds Ratio
3.00
2.50
2.00
1.50
1.00
0.50
0.00
-0.50
-1.00
-1.50
-2.00
-2.50
-3.00
-3.50
0.0
10.0
20.0
30.0
40.0
50.0
60.0
70.0
80.0
90.0
100.0
Cardiac Arrest

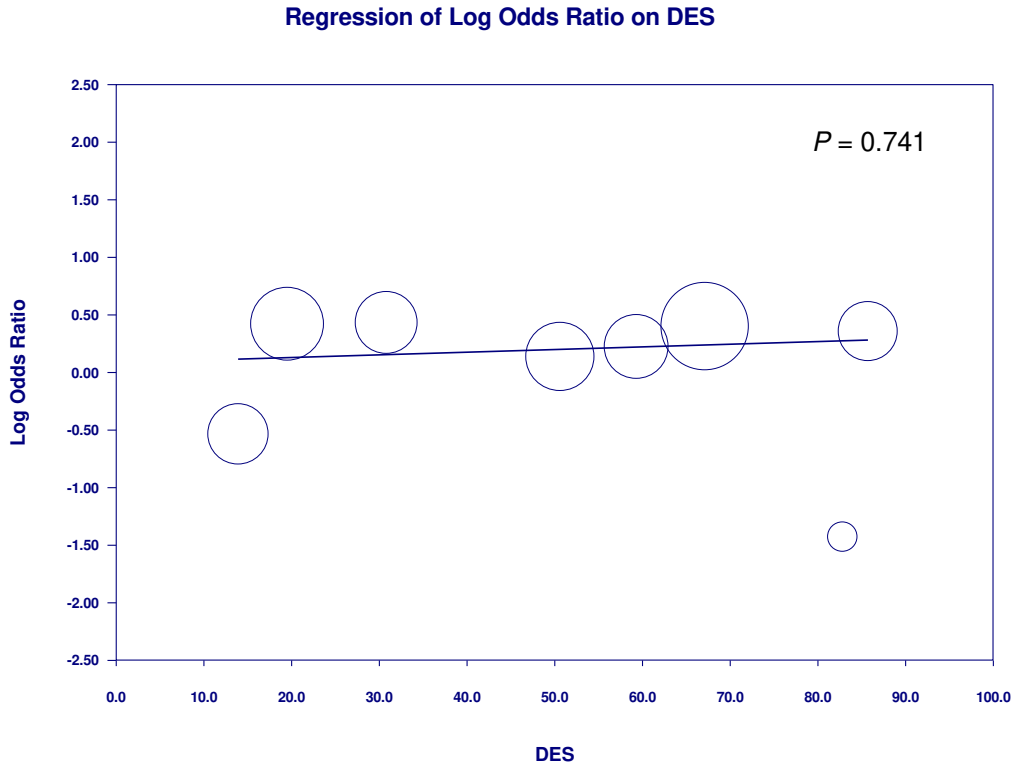
I)


Regression of Log Odds Ratio on LM/LAD Culprit
P = 0.815
Log Odds Ratio
5.00
4.00
3.00
2.00
1.00
0.00
-1.00
-2.00
-3.00
-4.00
-5.00
25.0
30.0
35.0
40.0
45.0
50.0
55.0
60.0
65.0
70.0
LM/LAD Culprit

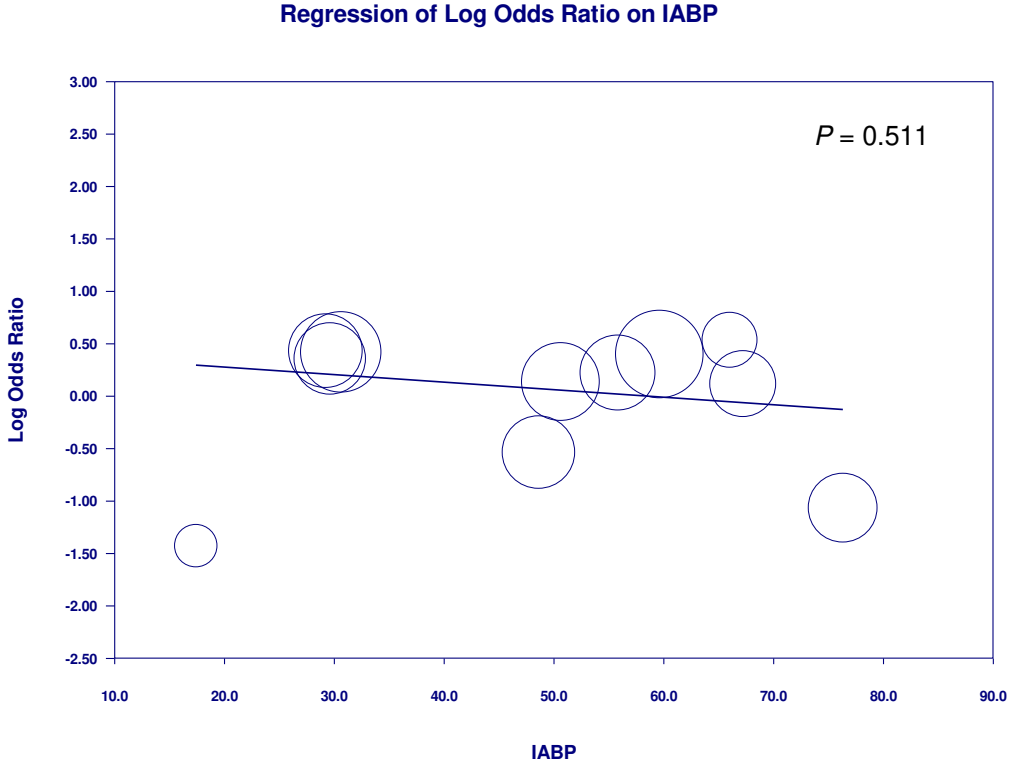
J)


Regression of Log Odds Ratio on Stent
P = 0.298
Log Odds Ratio
5.00
4.00
3.00
2.00
1.00
0.00
-1.00
-2.00
-3.00
-4.00
60.0
65.0
70.0
75.0
80.0
85.0
90.0
95.0
100.0
Stent

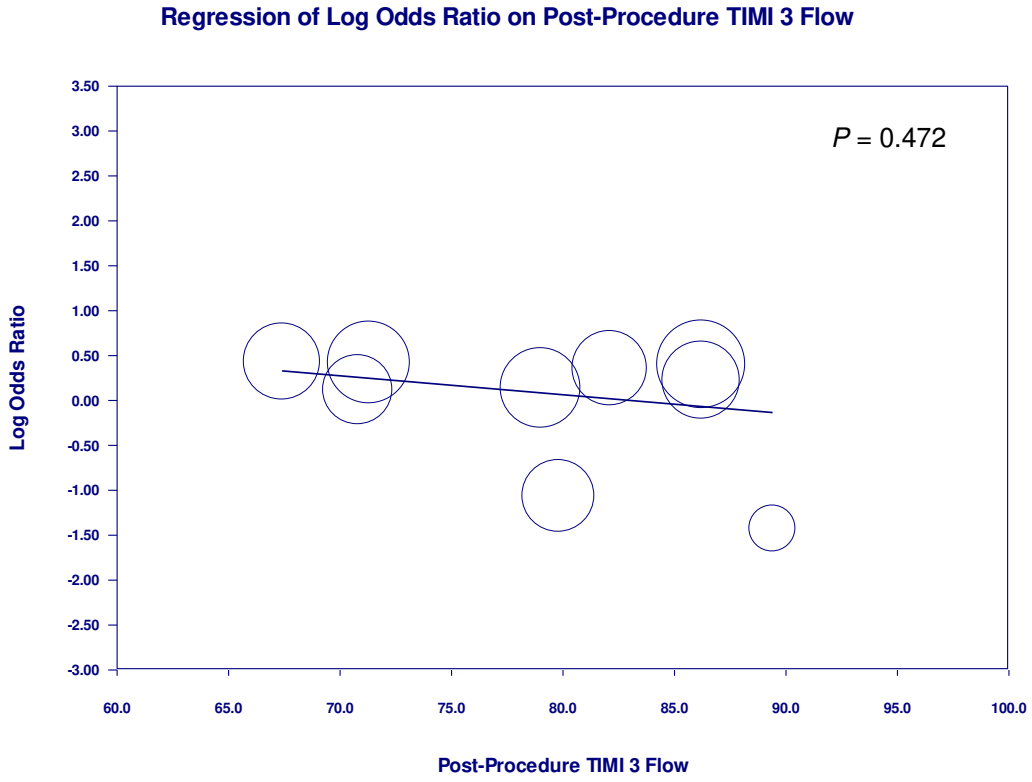
K)


Regression of Log Odds Ratio on DES
P = 0.741
Log Odds Ratio
2.50
2.00
1.50
1.00
0.50
0.00
-0.50
-1.00
-1.50
-2.00
-2.50
0.0
10.0
20.0
30.0
40.0
50.0
60.0
70.0
80.0
90.0
100.0
DES

L)


Regression of Log Odds Ratio on IABP
P = 0.511
Log Odds Ratio
3.00
2.50
2.00
1.50
1.00
0.50
0.00
-0.50
-1.00
-1.50
-2.00
-2.50
10.0
20.0
30.0
40.0
50.0
60.0
70.0
80.0
90.0
IABP

M)


Regression of Log Odds Ratio on Post-Procedure TIMI 3 Flow
P = 0.472
Log Odds Ratio
3.50
3.00
2.50
2.00
1.50
1.00
0.50
0.00
-0.50
-1.00
-1.50
-2.00
-2.50
-3.00
60.0
65.0
70.0
75.0
80.0
85.0
90.0
95.0
100.0
Post-Procedure TIMI 3 Flow

Supplemental References:

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